Recurrent brief depression revisited

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Summary

Recurrent Brief Depressive Disorder (RBD) is a well-defined and prevalent mood disorder with an increased risk of suicidal behavior and significant clinical impairment in the community and general practice. Occurring at least monthly with depressive episodes lasting only a few days defines recurrent Brief Depressive Disorder. The lifetime co-occurrence of both RBD and Major Depressive Disorder (MDD), called Combined Depression (CD), substantially increases the risk for attempted suicide, even more than that known for ‘pure’ MDD. The diagnostic criteria for RBD found in the ICD-10 and DSM-IV are helpful in research and clinical routine as well as several methodological issues, which make clinical diagnostic and drug response evaluation of RBD very different from MDD. Formal differences in the course of RBD and MDD require different designs for drug treatment studies. Denials of disorder, specific methodological requirements, and highly selected patient samples have probably been responsible for false negative results in double blind, placebo-controlled treatment studies. Although several authors reported successful treatment of RBD with different compounds in about 60 patients, it is still not possible to deduce a treatment algorithm for RBD to date. Obviously future treatment studies without the limitations of previous studies are clearly required for RBD. Results of ongoing studies will soon provide the first data on the biological underpinnings of RBD.

Introduction

Recurrent brief depressive episodes persisting for a few days and occurring spontaneously or triggered by mild psychosocial stressors, is a common psychiatric syndrome. These episodes are associated with substantial psychosocial impairment and an increased risk of suicidal behavior (Pezawas et al., 2003b).

Although the concept of Recurrent Brief Depression (RBD) was first published in 1984 (Angst & Dobler-Mikola, 1985), recurrent short-lived depressive episodes have been mentioned in psychiatric literature since the 19th century (Angst, 1994a).

History

In 1852 Pohl reported episodes of ‘periodic melancholia’ lasting hours to days (Angst, 1994a) and when Kraepelin published his pioneering work on ‘Manic-Depressive Illness’ in 1889, he even included psychopathological symptoms such as hypomanic or mild depressive moods of short duration in his concept (Angst, 1994a). In 1915 Gregory published a report on ‘Transient attacks of manic-depressive insanity’ (Angst, 1994a). He mentioned in detail the phenomenon of RBD: ‘Short attacks of a manic-depressive psychosis, ranging in duration from a few hours to several days, are very frequent’ and ‘...many sudden and unexpected suicides ... are due to fleeting attacks of a manic-depressive psychosis. I am led to this belief from the examination of hundreds of cases of attempted suicides’.

In 1929 Paskind underlined the clinical importance of brief depressions (Angst, 1994a). He was the first psychiatrist, who recognized that the majority of such patients are found more frequently in general health care settings than in psychiatric institutions. Read and Patrick confirmed the finding that recurrent brief depressions are significantly related to suicidal behavior (Angst, 1994a).

In 1955 Busse reported: ‘The depressive periods that we considered statistically had occurred at least once a month, and their duration had varied from a portion of an hour to a few days’ (Angst, 1994a). The subjects reported that these episodes of depression had not occurred in their younger years. Further
he noted: ‘… these episodes can be termed ‘reactive’
depressions’.

In the late 1970s Spitzer et al. (Angst, 1994a)
developed some psychiatric Research Diagnostic
Criteria, including a category called ‘intermittent
depressive disorder’, characterizing patients being
bothered for at least two years by depressed mood
(like in Minor Depression) lasting from hours to
about week and being in a normal mood in between.
However, this definition was rarely used after its
introduction. More recently, in 1980 Clayton et al.,
called such depressions ‘very brief depressions’,
which has not been adopted by the scientific com-
community either (Angst, 1994a). Similarly, in a study
performed by Montgomery and colleagues in
London (1989), which explores treatment options in
repeated suicide attempters with comorbid bor-
derline personality disorder, Montgomery et al.,
reported patients suffering from severe recurrent
brief depressive episodes being associated with
suicidal behavior. He called them ‘intermittent
three-day depressions’ (Montgomery, Montgomery,
Baldwin & Green, 1989). In his later work, he
substituted this descriptive term by the diagnostic
category of RBD (Montgomery, Green, Bullock,

In 1978, a longitudinal, epidemiological cohort
study of young adults assessing a continuum of
psychopathology from normal to disordered states
was launched in Zurich, Switzerland. The analysis of
the first follow-up interview showed the frequent
occurrence of depressive mood swings lasting less
than eight days (Angst & Dobler-Mikola, 1985).
Further research on this subject generated the first
operationalized definition of RBD, which has been
further revised (Angst, 1988). This definition of
RBD has been integrated in the ICD-10 system in

Finally, a seasonal variant of RBD has been added
to its clinical picture (Kasper, Ruhrmann, Haase &
Moller, 1992; Kasper, Ruhrmann, Haase &
Moller, 1994). See Table I for a summary of the
history of RBD.

### Epidemiology

Table II summarizes prevalence rates for RBD in
different epidemiological samples. So far RBD has
been independently investigated in two longitudinal
and two cross-sectional community samples. The
Zurich study (Angst & Dobler-Mikola, 1985) has the
longest observation period of a community sample in
the context of RBD, starting its investigation at the
age of 19 until the last interview performed at the age
of 41 in 1999. Recent data are currently being
analyzed (Pezawas et al., 2003a). This study revealed
a lifetime prevalence rate of pure RBD without mood
disorder comorbidity of 12.5%, which is similar to
pure MDD without mood disorder comorbidity with
a prevalence rate of 14.7%. In contrast, gender
distribution of RBD is distinct from MDD showing
a balanced sex ratio in RBD (1:1.3) and female excess
in MDD (1:16.3). Duration patterns in RBD and
MDD also differ significantly with a median duration
of brief depressive episodes of three days in RBD an
about 10 weeks in MDD (Angst, 1994b). However,
the cumulative number of depressive days per year
has been shown to be less significantly different
in RBD (43 days) and MDD (75 days) within
the Zurich study. In accordance with the Zurich
study, a community sample in Mainz exhibited
similar prevalence rates (Maier et al., 1994a). A
slightly lower prevalence rate of 7.6% has been
reported in a large study (n = 1040) in Sardina
(Carta et al., 2003). Recently, epidemiological find-
ings of RBD have been reinvestigated in a

### Table I. History of recurrent brief depression (RBD).

<table>
<thead>
<tr>
<th>Reference</th>
<th>Date</th>
<th>Finding</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pohl</td>
<td>1852</td>
<td>Described cases of multiple depressive episodes that lasted from hours to days; introduced the term ‘periodic melancholia’</td>
</tr>
<tr>
<td>Head</td>
<td>1901</td>
<td>Described cases of multiple depressive episodes that lasted from hours to days; association with ideas of suicide and impulse for self-destruction</td>
</tr>
<tr>
<td>Gregory</td>
<td>1915</td>
<td>Described cases of multiple depressive episodes that occurred independently from the menstruation cycle; association with suicide attempts and unexpected suicides</td>
</tr>
<tr>
<td>Paskind</td>
<td>1929</td>
<td>Observed episodes of RBD in elderly patients</td>
</tr>
<tr>
<td>Read, Patrick</td>
<td>1929</td>
<td>Increased suicidal behavior in brief depressions</td>
</tr>
<tr>
<td>Busse</td>
<td>1955</td>
<td>Found that 14% of patients with manic depression also suffered from RBD</td>
</tr>
<tr>
<td>Spitzer</td>
<td>1975</td>
<td>Attempted to operationalize an ‘intermittent depressive disorder’</td>
</tr>
<tr>
<td>Clayton</td>
<td>1980</td>
<td>Introduced the term ‘very brief depressions’</td>
</tr>
<tr>
<td>Angst</td>
<td>1985</td>
<td>Introduced the first operationalized diagnostic category of brief depressions based on the Zurich study, which he called RBD</td>
</tr>
<tr>
<td>Montgomery</td>
<td>1989</td>
<td>Studied psychiatric patients with repeated suicide attempts and borderline comorbidity; he introduced the term ‘intermittent 3-day depressions</td>
</tr>
<tr>
<td>Kasper</td>
<td>1992</td>
<td>Described a seasonal form of RBD</td>
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<tr>
<td>WHO</td>
<td>1992</td>
<td>Inclusion of RBD as diagnostic category in ICD-10</td>
</tr>
</tbody>
</table>
large community sample \((n = 3021)\) of adolescents and young adults within the Early Developmental Stages of Psychopathology Study (EDSP) in Munich, presenting prospective conservative estimations of findings on prevalence, incidence, clinical correlates, severity markers, comorbidity and course stability of RBD and other mood disorders (Pezawas et al., 2003b). Although this study applied conservative measures to the phenomenon of RBD, previous findings could be replicated in its core.

Support for community studies is also provided by a comprehensive World Health Organization (WHO) project on ‘Psychological Problems in General Health Care’ (PPGHC) and further associated studies in primary care settings (Sartorius et al., 1993). Notably two centers, Mainz (Maier et al., 1994a; 1994b) and Paris (Weiller, Boyer, Lepine & Lecrubier, 1994a) confirmed patterns of clinical significance in a cross-sectional study. Furthermore, prevalence rates of RBD are available for 15 different primary care centers \((n = 5438)\) in Brazil, Chile, Germany, France, Greece, India, Italy, Japan, the Netherlands, Nigeria, China, Turkey, UK, and the USA (Weiller, Lecrubier, Maier & Ustun, 1994b). A substantial number (3.7%) of investigated primary care seekers in a sample (including five centers) have been identified as suffering from RBD without mood disorder comorbidity. Another sample that included 10 centers \((n = 3527)\) using a slightly different definition of RBD found a 5.7% prevalence of RBD.

So far epidemiological studies provided similar findings on RBD demonstrating its significant prevalence in the community and primary care, and its clinical relevance.

### Diagnosis

In 1994, RBD was integrated as a new diagnostic category in ICD-10 (WHO, 1992a) and DSM-IV (American Psychiatric Association; APA, 1994) due to convincing epidemiological data (Table II). While RBD represents a distinct clinical diagnosis in ICD-10, DSM-IV classifies RBD into the subcategory of depressive disorders ‘Not Otherwise Specified (NOS)’. The DSM-IV manual offers operational diagnostic criteria for scientific use in the appendix but they do not qualify for clinical use due to numerous exclusion criteria. Psychopathological symptoms required for RBD are absolutely the same as for MDD. Therefore RBD cannot be thought \emph{a priori} to be a milder form of depression. As a matter of fact RBD can only be distinguished from MDD by the duration criterion (episode duration <14 days) and the frequency criterion (approx. one episode/month). In addition, the ICD-10 requires independence from the menstrual cycle and an observation period of one year. This also implies that RBD is not operationalized as a course specifier of MDD as it is the case for Seasonal Affective Disorder (SAD), for example.

### Clinical features

Reports of the depression symptom profile of RBD and MDD are provided by the Zurich and EDSP study (Pezawas et al., 2003b) showing similar patterns of depressive symptoms. Regarding symptoms reported in at least two thirds of subjects in the Zurich study (Pezawas et al., 2003a), it is intriguing

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Table II. Prevalence rates of RBD in the community.

<table>
<thead>
<tr>
<th></th>
<th>Sample size</th>
<th>Interview/method</th>
<th>Prevalence 1-year</th>
<th>Rates (%) lifetime</th>
</tr>
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<tr>
<td><strong>Community</strong></td>
<td></td>
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<tr>
<td>Sardinia</td>
<td>(n = 1024)</td>
<td>CIDI-S</td>
<td>–</td>
<td>7.6</td>
</tr>
<tr>
<td>age 18–65</td>
<td></td>
<td>cross-sectional</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Zurich study</td>
<td>(n = 367–591)</td>
<td>SPIKE</td>
<td>5.0–8.2</td>
<td>21.3</td>
</tr>
<tr>
<td>age 20–41</td>
<td></td>
<td>longitudinal</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mainz</td>
<td>(n = 317)</td>
<td>CIDI+</td>
<td>5.8</td>
<td>10.0</td>
</tr>
<tr>
<td>age 18–65</td>
<td></td>
<td>cross-sectional</td>
<td></td>
<td></td>
</tr>
<tr>
<td>EDSP study, Munich</td>
<td>(n = 3021)</td>
<td>CIDI-M</td>
<td>–</td>
<td>2.6*</td>
</tr>
<tr>
<td>age 14–24</td>
<td></td>
<td>longitudinal</td>
<td></td>
<td></td>
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<tr>
<td><strong>General practice</strong></td>
<td></td>
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</tr>
<tr>
<td>PPGHC study, Paris</td>
<td>(n = 405)</td>
<td>CIDI+</td>
<td>9.9</td>
<td>–</td>
</tr>
<tr>
<td>age 18–65</td>
<td></td>
<td>cross-sectional</td>
<td></td>
<td></td>
</tr>
<tr>
<td>PPGHC study, Mainz</td>
<td>(n = 300)</td>
<td>CIDI+</td>
<td>7.6</td>
<td>–</td>
</tr>
<tr>
<td>age 18–65</td>
<td></td>
<td>cross-sectional</td>
<td></td>
<td></td>
</tr>
<tr>
<td>PPGHC study, five centers</td>
<td>(n = 1911)</td>
<td>CIDI+</td>
<td>3.7</td>
<td>–</td>
</tr>
<tr>
<td>age 18–65</td>
<td></td>
<td>cross-sectional</td>
<td></td>
<td></td>
</tr>
<tr>
<td>PPGHC study, 10 centers</td>
<td>(n = 3527)</td>
<td>CIDI+</td>
<td>5.7</td>
<td>–</td>
</tr>
<tr>
<td>age 18–65</td>
<td></td>
<td>cross-sectional</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Family studies</strong></td>
<td></td>
<td></td>
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<td></td>
</tr>
<tr>
<td>Mainz</td>
<td>(n = 420)</td>
<td>CIDI+</td>
<td>7.4</td>
<td>14.6</td>
</tr>
<tr>
<td>age 18–65</td>
<td></td>
<td>cross-sectional</td>
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*Lower bound estimations.
that most symptoms have been reported less frequently in MDD in comparison to RBD. These data confirm the relevance of the diagnostic concept of RBD, demonstrating that RBD presents the full-blown picture of depression. Similar findings have also been reported in the EDSP study showing only slightly less frequent reported depression symptoms in RBD than MDD with the exception of sleeping problems, which appear to be higher in RBD (Pezawas et al., 2003b).

Within the Zurich study both RBD and MDD patients reported a 50% family history of any kind of depression (Pezawas et al., 2003a). This could be taken as an argument for placing RBD within the mood disorder spectrum. Suicide attempts were less frequently reported in RBD (10.2%) without mood disorder comorbidity, than in MDD (20.2%) in the Zurich study—similar to the results of the EDSP study (Pezawas et al., 2003b). However, general practice studies have revealed even higher suicide attempt rates: 16.1% in Mainz (Maier et al., 1994b), 23.3% in Paris (Weiller et al., 1994a), and 14% in five WHO centers (Weiller et al., 1994b). The relevance of suicidal behavior in RBD has also been supported by clinical studies (Montgomery et al., 1989; Pezawas et al., 2000) (Figure 1).

Furthermore, the concept of RBD and its clinical significance has been underlined by studies on patterns and consequences of a lifetime co-occurrence of both RBD and MDD, called Combined Depression (CD) (Figure 1), which was been introduced into psychiatric literature by Montgomery (Montgomery et al., 1989), and further developed by Angst (1990). Epidemiological (Angst & Hochstrasser, 1994; Maier et al., 1994b) and clinical (Angst & Hochstrasser, 1994; Maier et al., 1994b; Montgomery et al., 1989; Pezawas et al., 2002b) studies demonstrated a dramatic increase in suicide attempt rates and measures of impairment in cases of CD in comparison to either single RBD or MDD.

**Differential diagnosis**

The differential diagnosis of both clinical phenomena, RBD and MDD is based on their distinct course pattern of depressive episodes (1–3 days versus weeks or months).

From a clinical point of view it might be necessary to differentiate other psychiatric disorders mainly characterized by short-lived symptoms (Pezawas, Stamenkovic & Kasper, 2001). The list comprises:

1. Panic Disorder characterized by recurrent unexpected panic attacks. However, the attacks only last for minutes up to a few hours;
2. Premenstrual Dysphoric Disorder (PMDD) appearing exclusively in relation to the menstrual cycle. Premenstrual Dysphoric Disorder started in the last week of the luteal phase in most menstrual cycles recorded over a year. The symptoms begin to remit within a few days of the onset of menses (the follicular phase) and are always absent in the week following menses;
3. Borderline Personality Disorder (BPD), which in the case of affective instability, can be associated with depressive mood fluctuations that often persist for hours but also can last for days. But the following characteristic symptoms (according to the DSM-IV at least five symptoms) must be present in order to be able to diagnose a BPD: frantic efforts to avoid real or imagined abandonment, a pattern of unstable and intense interpersonal relationships, identity disturbance, impulsivity in areas that are potentially self-damaging, recurrent suicidal behavior, affective instability due to a marked reactivity of mood, chronic feelings of emptiness, inappropriate intense anger or difficulty controlling anger, transient stress-related paranoid ideation or severe dissociative symptoms. Low borderline personality disorder comorbidity has been found in our own clinical data (Pezawas et al., 2002b). Another clinical study reported similar low dimensional symptoms of personality disorders in RBD and PMDD (Berlin, Raju, Schmidt, Adams & Rubinow, 2001). Support also comes from a recent study demonstrating that endocrine responses to RBD and BPD differ substantially (De La Fuente, Bobes, Vizuete & Mendlewicz, 2002).
4. Rapid Cycling (RC) (> 4 episodes/year), Ultra-RC (episodes in a weekly rhythm) or Ultra-Ultra-RC (ultradian episodes) Bipolar
Disorders must show at least hypomanic (or manic) episodes according to DSM-IV (Kramlinger & Post, 1996). In the first case at least one depressive episode must last for at least 14 days and in the last case the episodes may not last longer than a day. Generally RC or Ultra-RC are prognostic bad course specifiers for Bipolar Disorder, which are developed by 15–20% (specifically RC) of bipolar patients (Post & Weiss, 1998b) and differentiating them from RBD rarely causes problems.

(5) Other affective disorders such as MDD, Minor Depression (according to DSM-IV), Bipolar Disorder, or Dysthymia can be easily distinguished from RBD by the criterion of duration of the depressive episode.

(6) Furthermore, it is necessary to distinguish RBD from Drug induced Depression as found in cocaine withdrawal, for example.

Recurrent brief depressive episodes have also been described in the presence of somatic diseases, for example, postictal dysphoria or the so-called interictal dysphoric disorder in epilepsy (Blumer, 2000). Recurrent brief depressive episodes have been reported to be associated with migraine plus aura (Merikangas, Merikangas & Angst, 1993). One study reported that about 70% of depressive episodes occurring in patients suffering from idiopathic Parkinson’s disease also meet the operationalized criteria for RBD (Wermuth et al., 1998). Furthermore, a case study of a patient suffering from Prader-Willi Syndrome, who also met diagnostic criteria of RBD has been reported (Watanabe, Ohmori & Abe, 1997), which is the only direct evidence available so far that RBD could be caused by genetic factors. Limited information is available if the phenomenon of RBD in elderly populations is distinct from RBD in younger cohorts (Heun, Muller, Freyberger & Maier, 1998; Heun, Papassotropoulos & Ptok, 2000). However, other aging studies that indicate lower prevalence rates of RBD (2.08%) in older cohorts are on their way (Maercker et al., 2003).

Course

The longitudinal course of mood disorders is characterized by a substantial diagnostic overlap within these diagnostic groups (Pezawas et al., 2003a). Therefore, longitudinal epidemiological studies like the Zurich study or EDSP study can provide data on some critical issues concerning the concept of RBD, evaluating the degree of evidence that is given to rule out that RBD is not only a prodromal or residual state of MDD or any other psychiatric disorder.

Both studies indicate that RBD is not a prodromal syndrome of MDD. The Zurich study indicated that RBD cases became MDD cases more often than vice versa. About 10% of all initially diagnosed MDD cases developed RBD during follow-up and 20% vice versa. This phenomenon was hypothetized as ‘kindling-phenomenon’ by Angst (1994b) and is in accordance with biological models dealing with the longitudinal development of mood disorders (Post & Weiss, 1998b).

Concerning the hypothesis that RBD might be a residual state of MDD, both studies found that only a limited proportion of subjects developed RBD after being diagnosed as MDD, which provides evidence that RBD is not merely a residual state of MDD. Hence the diagnostic stability over time is similar for RBD and MDD.

Treatment

Two thirds of all RBD patients seek professional help in the course of their life (Angst, 1994b). One quarter consult the general practitioner, one quarter see a psychologist and the remaining half consult a psychiatrist or neurologist. In the Zurich study, almost all of these patients were stated as having received psychotherapy treatment (Angst, 1994b). However, RBD patients hardly ever receive pharmacological medication. The PPGHC study revealed that the prescription rate of psychotropic substances for patients with RBD in general practice was 19%. This rate was the lowest and was three times lower than the rate for patients with agoraphobia (Linden et al., 1999). Furthermore, a substantial number of patients with RBD that received previous treatment frequently have a history of inadequate therapeutic response to different pharmacological treatment strategies normally offered by their general practitioner (Kasper, Stamenkovic & Pezawas, 2000). The fact that about 10% of all ‘pure’ RBD patients and about 30% of all patients with a lifetime co-occurrence of RBD and MDD (combined depression) in the Zurich study attempted suicide during the two decades of observation underlines the need for sufficient treatment.

Almost two decades after the conceptualizing of RBD, clinical trials concerning psychotherapy, as well as biological treatment strategies (e.g., light therapy), still have not been carried out, although patients suffering from RBD frequently undergo psychotherapy (Angst, 1994b). There is only one case study about a patient suffering from a seasonal type of RBD that describes the induction of ultradian rapid cycling after light therapy (Meesters & Van Houwelingen, 1998).

However, there are a few placebo-controlled studies (Table III) and several case reports, a
suicide attempts; csingle case analysis; dParkinson patients with RBD; eCarbamazepine was prescribed as add-on treatment to nimodipine; fresponse to treatment; gPazzaglia et al., 1998c; hNimodipine was reported by successful results found in double-blind placebo-controlled one-tailed single case analyses and two-tailed studies assessing treatment of patients with RBD. Anyhow, this presumption is supported by successful results found in double-blind placebo-controlled one-tailed single case analyses with nimodipine, verapamil, and carbamazepine (Pazzaglia, Post, Ketter, George & Marangell, 1993; Pazzaglia et al., 1998). However, controlled studies were carried out with highly selected RBD patient samples for example, patients with repeated suicide attempts or comorbid borderline personality disorder or somatic diseases (Kocmur, Dernovsek & Tavcar, 1998; Montgomery et al., 1994; Verkes et al., 1998; Wermuth et al., 1998), and this might have led to a bias directed towards therapy resistance. Our own positive experience concerning treatment with mirtazapine (Stamenkovic, Pezawas, De Zwaan, Aschauer, & Kasper, 1998), reboxetine (Pezawas et al., 2002a), and fluoxetine, as well as other positive results from case reports with lithium (Corominas et al., 2002a), tranylcypromine (Malt & Fladvad, 2001) and tranylcypromine (Joffe, 1996) put the negative findings from other studies due to the above mentioned reasons in question (Pezawas et al., 2001).

In any case, to date, it is not possible to derive a specific treatment strategy for RBD from the existing data. Because the study results remain unclear and contradictory, there is a great need for future controlled clinical trials without the methodical limitations of previous studies. Taking into consideration that to date, successful treatment of RBD has been reported for about 60 patients, a first choice antidepressant treatment attempt with substances lacking severe side effects seems to be justified.

Future perspectives

Recurrent Brief Depressive Disorder originated from epidemiological research, which distinguishes this disorder from any other psychiatric disorder. So far epidemiologic studies were able to elaborate clinical features of RBD and estimate prevalence rates in different populations. A substantial new piece of information will be provided by new data of the EDSP study, which included a parental psychiatric interview as well as information on the early developmental symptoms of their offspring. These data (Pezawas et al., in preparation) demonstrate that parents of RBD patients do not exhibit higher rates of MDD than the normal population. This is a surprising finding since MDD rates of parents of MDD patients are dramatically elevated and support the idea that MDD has a substantial genetic component in its etiology. Our data suggests that there might be a substantial difference between the genetic risk factors of MDD and RBD. Furthermore, these data demonstrates that RBD patients are essentially more exposed to stress-related life events than MDD patients.

The pessimism concerning the treatment of RBD might be unjustified, due to false negative study results. Recent progress has been made in the

<table>
<thead>
<tr>
<th>Investigator</th>
<th>n</th>
<th>Treatment</th>
<th>Response</th>
</tr>
</thead>
<tbody>
<tr>
<td>Kocmur et al., 1998a</td>
<td>16</td>
<td>Paroxetine</td>
<td>–</td>
</tr>
<tr>
<td>Kasper et al., 2000</td>
<td>148</td>
<td>Paroxetine</td>
<td>–</td>
</tr>
<tr>
<td>Montgomery et al., 1994</td>
<td>107</td>
<td>Fluoxetine</td>
<td>–</td>
</tr>
<tr>
<td>Kasper et al., 2000</td>
<td>37</td>
<td>Flupenthiole</td>
<td>–</td>
</tr>
<tr>
<td>Montgomery et al.</td>
<td>58</td>
<td>Mianserin</td>
<td>–</td>
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<tr>
<td>Pazzaglia et al., 1998</td>
<td>2</td>
<td>Carbamazepine</td>
<td>+</td>
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<td>Nimodipine</td>
<td>+</td>
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</tr>
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<td>Wermuth et al., 1998b</td>
<td>37</td>
<td>Citalopram</td>
<td>–</td>
</tr>
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<thead>
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<th>Investigator</th>
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<th>Treatment</th>
<th>Response</th>
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<tr>
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<td>Fluoxetine</td>
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<tr>
<td>Corominas et al., 1998</td>
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<td>Clomipramine</td>
<td>–</td>
</tr>
<tr>
<td>Corominas et al., 1998</td>
<td>1</td>
<td>Lithium</td>
<td>+</td>
</tr>
<tr>
<td>Gertz, 1992a</td>
<td>1</td>
<td>Amitryptiline</td>
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</tr>
<tr>
<td>Gertz, 1992a</td>
<td>1</td>
<td>Carbamazepine</td>
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<tr>
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<td>Clomipramine</td>
<td>–</td>
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<tr>
<td>Gertz, 1992a</td>
<td>1</td>
<td>Maprotiline</td>
<td>–</td>
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<tr>
<td>Gertz, 1992a</td>
<td>2</td>
<td>Tranylcypromine</td>
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<td>2</td>
<td>Mirtazapine</td>
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prospective assessment of mood symptoms in such rapid cycling depressive mood disorders like RBD. It has been worked out that designs and statistical methods used in clinical studies in the past have been insufficient. However, several questions remain concerning the optimal clinical study design, instruments for assessing RBD symptoms, and appropriate statistical methods. Future efforts in the field of RBD should also include these methodological aspects.

The optimal treatment regime for RBD remains an open question. Based on information from treatment studies, a prescription with modern antidepressants seems to be appropriate. As a second line treatment, mood stabilizers can be considered. However, longer response rates (weeks to a few months) than those seen in MDD are characteristic for this disorder since symptoms occur less frequently than in MDD.

Finally, there is very limited information available on the biological features of RBD due to a lack of ‘pure’ RBD patients in psychiatric institutions. Supportive data might soon be available from tryptophan depletion studies in Vienna and electrophysiological, structural and functional imaging studies in Oslo (Malt, 2003).

Summarizing progress in RBD research, we conclude that RBD is an epidemiological well-characterized disorder that is common in primary care and in the community, but less common in psychiatric practice. Therefore, clinical studies are lacking in the field of RBD research today and further studies are clearly needed. The pessimism concerning the drug treatment for this disorder (originating from the first studies) seems to be inappropriate today. Progress in methods, which should be used for the assessment and evaluation of this disorder, may contribute to the development of better treatment strategies for this disorder.

References


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