

# Emotra EDOR<sup>®</sup>

**Scientific background for the EDOR-Test**

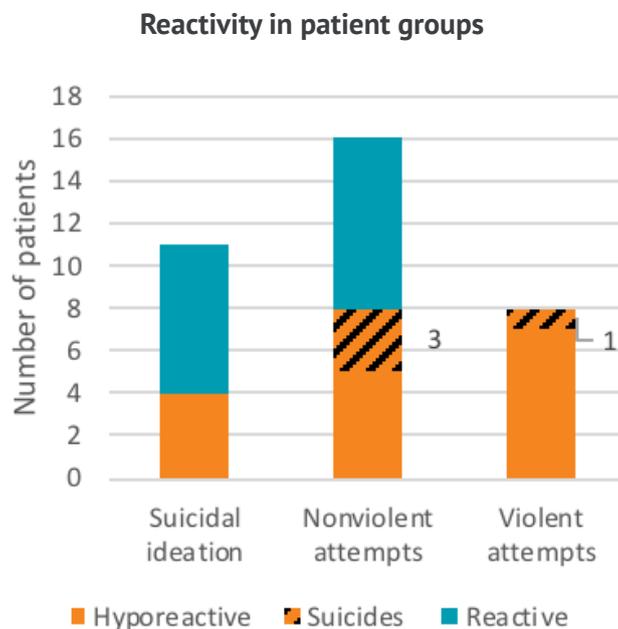


## FROM DISCOVERY TO CLINICAL ROUTINE

The Journey for EDOR started with a small, blind study in the mid-eighties and has since then gained more evidence as a method for detecting hyporeactivity as a risk factor for suicide in patients with primary depression. In this document, the most important studies connected to the EDOR-method are presented and explained.

The first study<sup>1</sup> was made 1986 at a research ward at Karolinska Hospital in Stockholm. It was a blind study, where patients were included by the psychiatrist on duty when classified as depressed, suicidal and drug-free. Patients ( $n=23$ ) were tested for 5-HIAA in liquor and electrodermal habituation, where fast habituators are hyporeactives and all others, are called reactive.

Electrodermal reactivity measurements showed 15 reactive and 16 hyporeactive patients with a bimodal distribution that was statistically significant.



*Reactivity and suicides per patient group. Ref: Edman Et Al. Skin conductance habituation and cerebrospinal fluid 5-hydroxyindoleacetic acid in suicidal patients. Arch Gen Psychiatry. 1986; 43:586–592.*

One year later, a follow-up was made showing four suicides; one with violent suicide method and three having non-violent suicide attempts, while none in patients with ideation. All suicides were hyporeactive (28.6% suicide rate), while none of the reactive patients (0%) committed suicide. Here, it was first discovered that hyporeactivity could be associated with suicide and suicide attempts, and that it was independent from 5-HIAA in liquor.

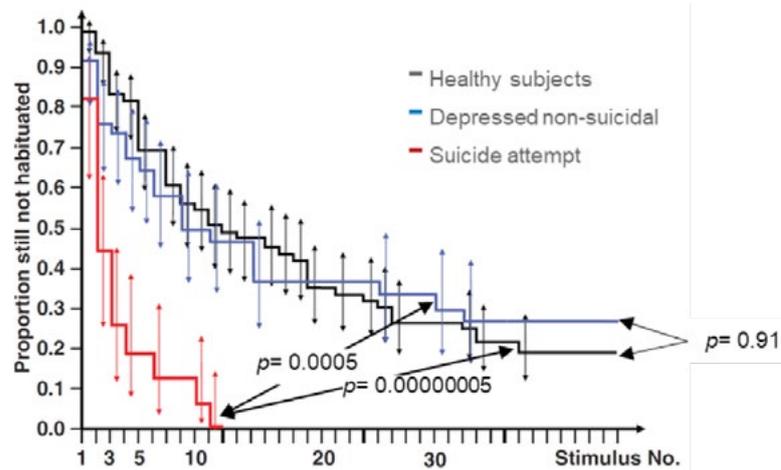
In parallel to the first published paper, another study<sup>2</sup> was running at the psychiatric department at Linköping University. It was initiated because of the many times repeated findings of lower electrodermal activity in depressed subjects that had been seen for the first time almost a century ago.

Here, patients ( $n=59$ ) were almost all inpatients in a blinded study design with inclusion criteria classified as depressed according to DSM III. Electrodermal reactivity was measured according to the special habituation experiment and patients were rated clinically using two clinical scales; CPRS and GAS.

The share of subjects in different groups who responded to stimuli was plotted (responsivity curve), showing a significant difference between suicide attempters and non-suicidal depressed

patients (see Figure). The responsivity curves also showed a great similarity in non-suicidal patients and healthy subjects. Electrodermal reactivity was not significantly related to the severity of symptoms of depression (CPRS), or the severity of general psychological disturbances (GAS).

### Responsivity curves



*Electrodermal responsivity in different groups. Ref: Thorell Et Al. Electrodermal activity in antidepressant medicated and unmedicated depressive patients and in matched healthy subjects. Acta Psychiatrica Scandinavica 1987;76:684-692.*

A one-year follow-up period revealed overall two suicides (3.4%), all in the group of hyporeactives (8.0%) while none in reactive (0%) subjects. This finding corroborated the results found in the previous study.

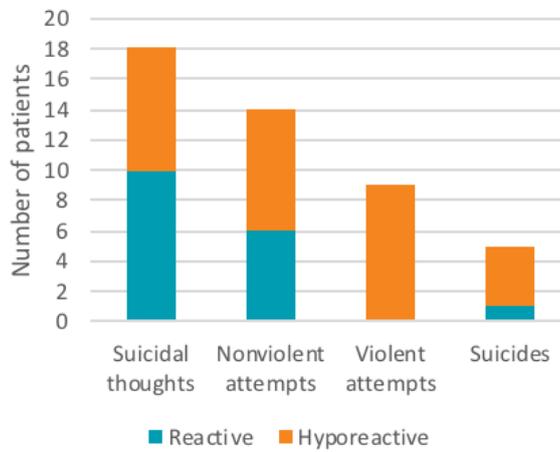
Another study on electrodermal reactivity in depressed patients was running during 17 years at the depression ward in Weissenau, Germany. Over time, this led to a build-up of patient records serving as a basis for research on reactivity, depression and suicide.

As a part of that study, a paper<sup>3</sup> was published using a sample of approximately 100 depressed inpatients with information on suicidality. The material used three matched groups, 18 subjects in each:

- Non-suicidal patients
- Suicidal ideators
- Suicide attempters

A total of five suicides were noted; four hyporeactive and one reactive. The reactive patient was excluded from the statistical analyses because of being in a state of drug withdrawal. Analysis of reactivity between ideators, violent and non-violent attempters showed that there was a statistically significant difference across all three groups.

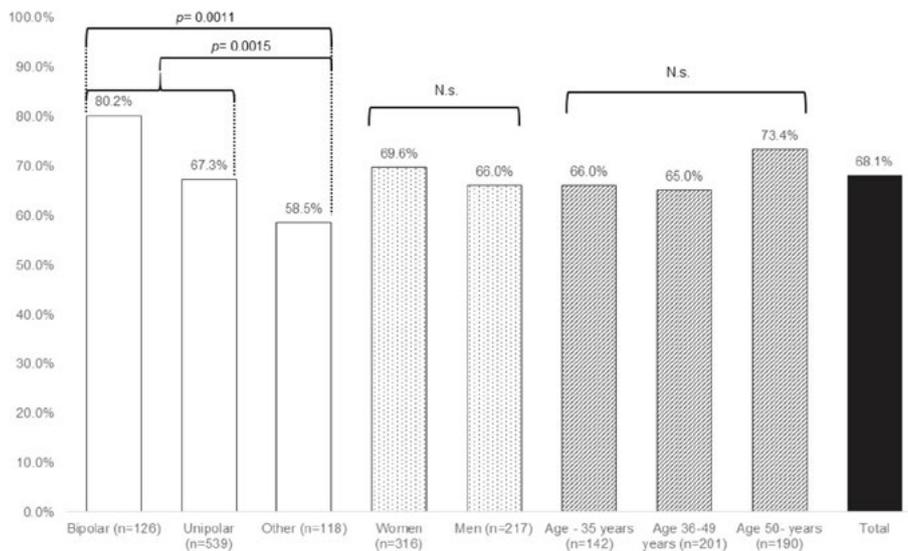
**Reactivity per patient group and in suicides**



*Electrodermal reactivity and suicides in patient groups. Ref: Keller F, et al. Suicidal behaviour and electrodermal activity in depressive inpatients. 1 Acta Psychiatr Scand 1991; 83: 324-328.*

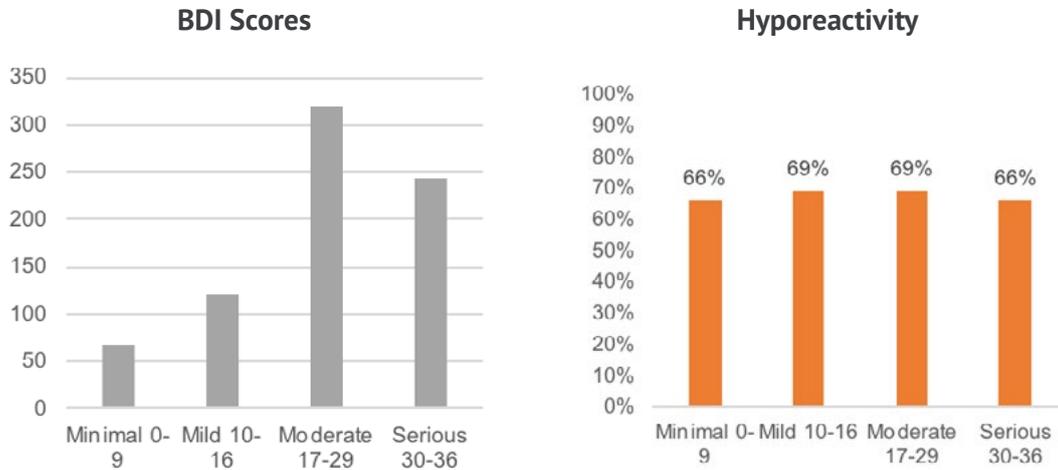
The whole material in the large 17-years study was not analysed until 2011. Thorell was offered the opportunity to do that which resulted in the next paper<sup>4</sup>. This study was partly blind since only the researchers knew the results, and only a few clinicians used it in their suicide risk assessments. Records of 783 depressed inpatients were analysed with EDR including clinical scales as Beck Depression Inventory (BDI) and STAI-Trait scale for trait anxiety.

Analysis showed 250 reactive patients and 533 hyporeactive. Prevalence of hyporeactivity did not differ between age groups or gender, which agrees with results from previous research. Bipolar patients had the highest prevalence of hyporeactives, followed by unipolar patients.



*Prevalence of hyporeactivity in patient groups, age, gender and total. Ref: Thorell Et al. Electrodermal hyporeactivity as a trait marker for suicidal propensity in uni- and bipolar depression. J. Psychiatr. Res. 2013;47:1925-1931.*

For clinical the scales, results confirmed a lack of correlation between ratings from clinical scales vs. the distribution of hyporeactivity. Hyporeactivity showed a very consistent share of hyporeactives across the different BDI-scores, ranging from minimal to serious classification.

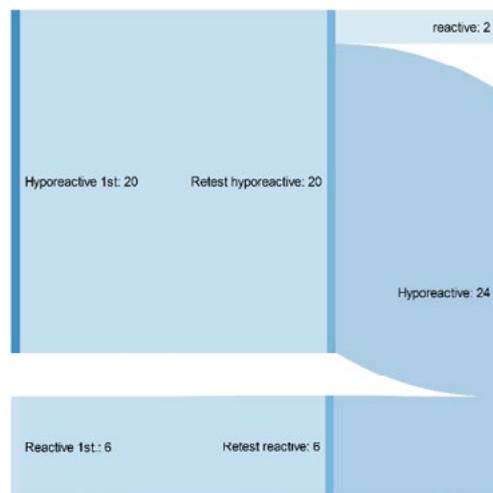


Hyporeactivity shown to be independent of total BDI-scores. Ref: Thorell Et al. Electrodermal hyporeactivity as a trait marker for suicidal propensity in uni- and bipolar depression. J. Psychiatr. Res. 2013;47:1925–1931.

Due to the 17 years long duration of the study 26 patients were tested twice, with time between tests varying from 0 to 12 years.

In this data, it could be shown that patients with recurrent depressions most often remain hyporeactive, and that reactive patients are prone to become hyporeactive. Out of 20 hyporeactive patients, 2 became reactive and all 6 reactive became hyporeactive, resulting in a total of 24 hyporeactives. This result, and the result from the paper by Thorell<sup>2</sup> indicate that hyporeactivity is a time extended condition that can last for many years.

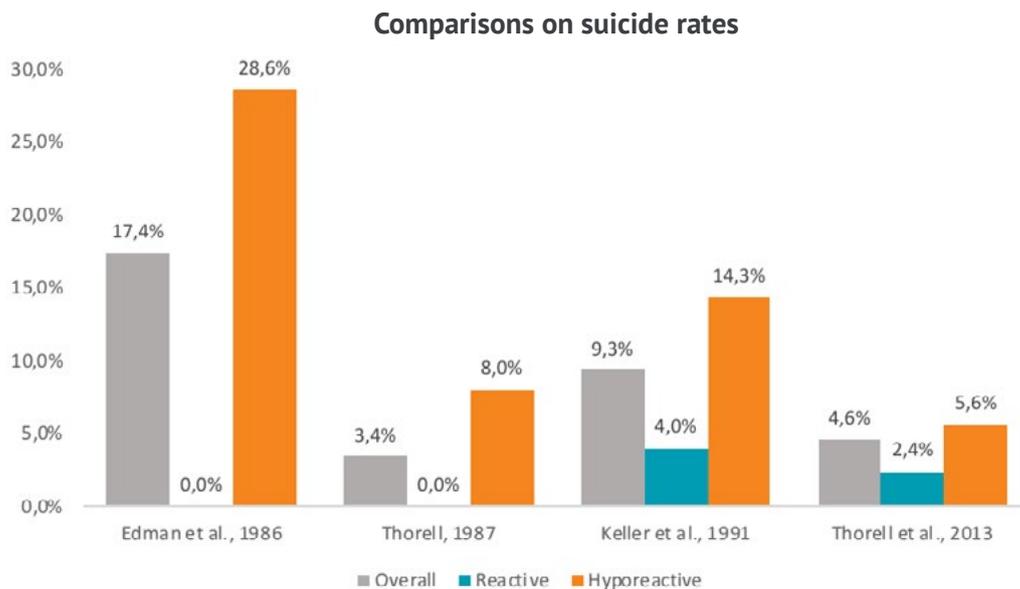
In total, 36 suicides were recorded. Overall suicide rate was 4.6%, while for hyporeactives 6.2% and reactive 2.0%. Conclusion was that hyporeactivity is a marker for suicidal propensity in uni- and bipolar depression.



Electrodermal reactivity after re-test of patients. Ref: Thorell Et al. Electrodermal hyporeactivity as a trait marker for suicidal propensity in uni- and bipolar depression. J. Psychiatr. Res. 2013;47:1925–1931.

By now, a series of studies had established a clear pattern (see graph below) on suicide rates and hyporeactivity:

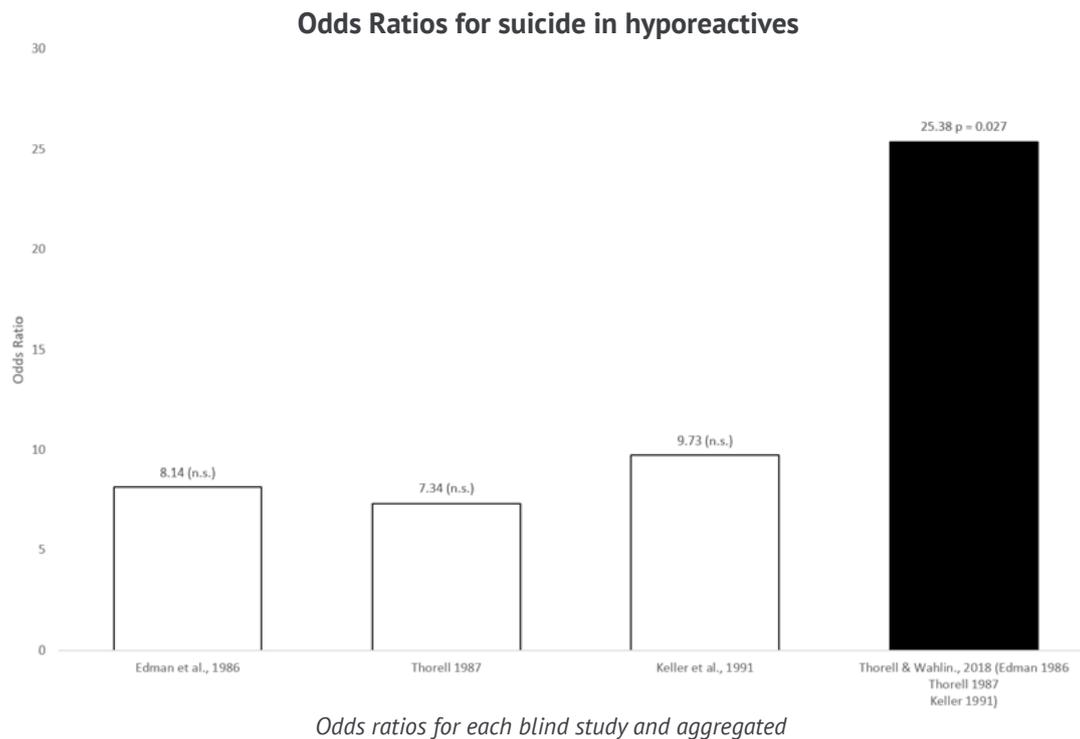
- Suicides are overrepresented in the group of Hyporeactives, functioning as a risk marker for suicide and violent suicide attempts
- Hyporeactivity as a marker, is independent of gender, age and commonly used clinical scales on depressive symptoms and general psychological disturbance.
- Hyporeactivity varies with the share of bipolar, unipolar and other types of mood disorders.



*Summary of suicide rates based on reactivity.*

However, all studies had been made either in controlled environments or at specific clinics. To study the effects of implementing the EDOR-test in clinical routine, a large, open and naturalistic multicentre study was initiated – the EUDOR-A<sup>5</sup>. This is now an ongoing project, expected to be submitted during 2018.

In a continuing effort to clarify the association between hyporeactivity and suicide risk, a new study was made by Thorell and Wahlin. This study was based on an aggregation of three previously conducted blind studies showing that hyporeactivity is a strong and clear biomarker for suicide risk.



First of all, the results show that the disproportional distribution of suicides among hyporeactive patients is not a coincidence ( $p=0.00058$ ). Secondly, the study shows that the suicide risk associated with hyporeactivity is 25 times higher (Odds Ratio = 25.38) compared with patients in the reactive group. These new results demonstrate that hyporeactivity is a clear and strong marker for suicide risk.

Another important conclusion that can be drawn from the study results is that depressed patients whose tests show they are normally reactive belong to a group that is significantly less susceptible to suicide attempts than the average patient who seeks care for depression.

## REFERENCES

- 1, Edman G, Åsberg M, Levander S, Schalling D. Skin conductance habituation and cerebrospinal fluid 5-hydroxyindoleacetic acid in suicidal patients. *Arch Gen Psychiatry*. 1986; 43:586–592.
- 2, Thorell LH, Kjellman BF, d’Elia G. Electrodermal activity in antidepressant medicated and unmedicated depressive patients and in matched healthy subjects. *Acta Psychiatrica Scandinavica* 1987;76:684-692.
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- 4, Thorell LH, Wolfersdorf M, Straub R, Steyer J, Hodgkinson S, Kaschka WP, et al. Electrodermal hyporeactivity as a trait marker for suicidal propensity in uni- and bipolar depression. *J. Psychiatr. Res.* 2013;47:1925–1931.
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- 6, Thorell, Wahlin, “Electrodermal Hyporeactivity as a Marker for Vulnerability to Suicide in Depression”, *EC Psychology and Psychiatry*, Volume 7 Issue 10, October 01, 2018.