A radical shift in the treatment of child and adolescent depression
Perhaps the time is ripe?

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With Peter Fonagy and Liz Allison
Overview

Have we hit the ceiling in the treatment of youth depression?

A new take on treatment:
- P-factor
- Epistemic trust and salutogenesis
- Domains of functioning in youth depression

Implications for clinical practice:
- How we treat young people with depression
- Where we treat young people with depression

Why have we forgotten about the environment???

I didn’t know which stick you threw, so I got them all.
"Failure: the essence of our profession"

Between the lines of the interview, professor Luyten voices the psychotherapeutic attitude by commenting on failure: "This is actually the essence of our profession. We all fail on a daily basis. Instead of feeling like a failure constantly, we might want to start learning from our faults. If there is one thing that I have learned in the past decade or so, it is from my treatment failures. When we do well, it probably has more to do with the patient than with us. Patients often improve, even despite us. But if treatment fails, we can really learn what it entails to be more effective."

European Society for Child & Adolescent Psychiatry (ESCAP) KEYNOTE LECTURE ON CHILDHOOD DEPRESSION
Patrick Luyten  www.escap.eu
Selective Trust!
Why we need to know how psychotherapy leads to change

• A few mechanisms might explain many treatments

• We need to know what components to improve and what components must not be diluted

• May help us identify moderators of treatment (variables on which effectiveness may depend)


What we increasingly realize

- Different treatments are supported by evidence that they produce change.
- It is unlikely that these treatments “cut nature at its joints”:
  - Common brain and psychosocial mechanisms
  - NIMH RDoC initiative
- If research on outcomes improves intervention techniques then therapies should have in general increased in effectiveness.
Evidence-based treatments for depression in adults
The “Dodo Bird Verdict”

“everybody has won and must have prizes”

- Psychotherapies are better than no treatment
- Psychotherapies are better than medication
- All psychotherapies have similar outcomes

APA, 2012; Zuroff et al., 2010; Lutz et al., 2007
The “Dodo Bird Verdict”

- Meta-analysis of high quality RCTs comparing PDT and CBT
- N=23 trials, totaling 2,751 patients
- Depression, anxiety, PTSD, eating disorders, substance-related disorders, personality disorders
- Equivalence tested using Two One-Sided Test (TOST) procedure with small effect size difference \((d=.25)\) as equivalence margin
- No evidence for researcher allegiance

The “Dodo Bird Verdict”

Hedges $g = -0.15$ (90% CI -0.227 - 0.079) at posttreatment

Hedges $g = -0.049$ (90% CI -0.137 - 0.038) at follow-up

FIGURE 1. Analysis of Effects of Psychodynamic Therapy Relative to Established Comparators on Target Symptoms at Posttreatment

<table>
<thead>
<tr>
<th>Study</th>
<th>Comparison</th>
<th>Hedges’ $g$ and 95% CI</th>
<th>Relative Weight (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Barber et al. (52)</td>
<td>PDT vs. Med</td>
<td></td>
<td>3.46</td>
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<td>Connolly Gibbons et al. (51)</td>
<td>PDT vs. CBT</td>
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<td>Cooper et al. (53)</td>
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<td>Driessen et al. (46)</td>
<td>PDT vs. CBT</td>
<td></td>
<td>9.53</td>
</tr>
<tr>
<td>Gallagher-Thompson and Steffen (54)</td>
<td>PDT vs. CBT</td>
<td></td>
<td>2.17</td>
</tr>
<tr>
<td>Salminen et al. (55)</td>
<td>PDT vs. Med</td>
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<td>2.17</td>
</tr>
<tr>
<td>Shapiro et al. (56)</td>
<td>Combined</td>
<td></td>
<td>2.75</td>
</tr>
<tr>
<td>Thompson et al. (57)</td>
<td>Combined</td>
<td></td>
<td>2.16</td>
</tr>
<tr>
<td>Bögels et al. (58)</td>
<td>PDT vs. CBT</td>
<td></td>
<td>1.96</td>
</tr>
<tr>
<td>Leichsenring et al. (59)</td>
<td>PDT vs. CBT</td>
<td></td>
<td>19.54</td>
</tr>
<tr>
<td>Leichsenring et al. (60)</td>
<td>PDT vs. CBT</td>
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<td>2.76</td>
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<td>Milrod et al. (61)</td>
<td>PDT vs. CBT</td>
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<td>6.09</td>
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<td>Brom et al. (62)</td>
<td>PDT vs. CBT</td>
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<td>2.52</td>
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<td>Garner et al. (63)</td>
<td>PDT vs. CBT</td>
<td></td>
<td>2.32</td>
</tr>
<tr>
<td>Poulsen et al. (64)</td>
<td>PDT vs. CBT</td>
<td></td>
<td>2.38</td>
</tr>
<tr>
<td>Tasca et al. (65)</td>
<td>PDT vs. CBT</td>
<td></td>
<td>3.54</td>
</tr>
<tr>
<td>Zipfel et al. (66)</td>
<td>PDT vs. CBT</td>
<td></td>
<td>5.30</td>
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<td>Crits-Christoph et al. (67)</td>
<td>Combined</td>
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<td>5.89</td>
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<tr>
<td>Woody et al. (68)</td>
<td>PDT vs. CBT</td>
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<td>3.16</td>
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<tr>
<td>Clarkin et al. (69)</td>
<td>Combined</td>
<td></td>
<td>1.22</td>
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<tr>
<td>Emmelkamp et al. (70)</td>
<td>PDT vs. CBT</td>
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<td>1.91</td>
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<tr>
<td>Muran et al. (71)</td>
<td>Combined</td>
<td></td>
<td>1.81</td>
</tr>
<tr>
<td>Svartberg et al. (72)</td>
<td>PDT vs. CBT</td>
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<td>2.39</td>
</tr>
</tbody>
</table>

Overall

Random effects Hedges’ $g = -0.153$
Heterogeneity: $\chi^2=17.99$, df=22, $p=0.71$, I$^2=0.0018$
(90% equivalence CI=--0.227 to --0.079)
Test for equivalence: $z_1=2.15$, $z_2=-8.94$; $p=0.016$

$^a$ CBT=cognitive-behavioral therapy; Med=pharmacotherapy; PDT=psychodynamic therapy.
Dodo Bird Verdict in Depression
The “Dodo Bird Verdict” in depression

Short-term psychodynamic therapy for depression

META-ANALYSIS

N=54 studies, totaling 3,946 patients

No significant differences found between brief PDT and other therapies at post-treatment
\( (d = -0.14) \)

No significant differences found between brief PDT and other therapies at follow-up
\( (d = -0.06) \)

Cognitive Behavioral Therapy (CBT) vs. Psychodynamic Therapy (PDT) for Major Depression (N=341)

- **CBT**
  - 16 individual sessions
  - Manualised (Molenaar et al., 2009)
  - N=164

- **Psychodynamic Therapy**
  - 16 individual sessions
  - Manualised (de Jonghe, 2005)
  - N=177

Humanistic-experiential therapies

Total: $g = .08$

Active $g = -.10$ ; TAU $g = .51$

Sharbanee, Elliott, & Bergmann, 2017
Improving Access to Psychological Therapies (IAPT)

April 2014 - March 2015:

**1,267,193 referrals**

815,665 referrals entered treatment;

*for which* 32.0 days was the average (mean) waiting time

1,123,002 referrals ended;

*of which* 468,881 (41.8%) finished a course of treatment;

*for which* 6.3 was the average (mean) number of attended treatment appointments
Improving Access to Psychological Therapies (IAPT)

Figure 3: Recovery rates by therapy type for referrals with a problem descriptor of depression, 2014/15

- Interpersonal Psychotherapy (IPT): 53.9%
- Couples Therapy: 52.0%
- Guided Self Help: 47.8%
- Brief psychodynamic psychotherapy: 47.0%
- Counselling: 45.2%
- Other HI: 45.1%
- Behaviour Activation: 44.8%
- Cognitive Behavioural Therapy (CBT): 44.1%
- Psychoeducational peer support: 43.0%
CBT vs. PDT for Major Depression (N=341)

Remission and Response Rates

<table>
<thead>
<tr>
<th>Therapy</th>
<th>Remission Rate (%)</th>
<th>Response Rate (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>CBT</td>
<td>24.300</td>
<td>38.700</td>
</tr>
<tr>
<td>PDT</td>
<td>21.300</td>
<td>36.900</td>
</tr>
</tbody>
</table>

Moderately depressed patients
No differences between therapies

Severely depressed patients in dual therapy
No differences between therapies

Lower remission rates for both therapies could be explained by the sample’s low SES and Axis I comorbidity!

Driesen et al., 2012
## CBT vs. PDT for Major Depression (N=341)

### Additional treatments during 1 year follow-up

<table>
<thead>
<tr>
<th>Treatment</th>
<th>CBT Percentage</th>
<th>PDT Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>CBT, Psychotherapy</td>
<td>34.800%</td>
<td>25.000%</td>
</tr>
<tr>
<td>CBT, Antidepressants</td>
<td>9.800%</td>
<td>9.300%</td>
</tr>
<tr>
<td>CBT, Day-treatment</td>
<td>0.000%</td>
<td>2.200%</td>
</tr>
<tr>
<td>CBT, Other</td>
<td>8.000%</td>
<td>3.500%</td>
</tr>
<tr>
<td>PDT, Psychotherapy</td>
<td>9.800%</td>
<td>25.000%</td>
</tr>
<tr>
<td>PDT, Antidepressants</td>
<td>9.300%</td>
<td>9.300%</td>
</tr>
<tr>
<td>PDT, Day-treatment</td>
<td>1.000%</td>
<td>2.200%</td>
</tr>
<tr>
<td>PDT, Inpatient treatment</td>
<td>0.000%</td>
<td>0.000%</td>
</tr>
</tbody>
</table>

Driesen et al., 2012
Publication bias?


Fig. 2 Funnel plots. (a) All psychotherapy studies, without imputed studies; (b) studies of cognitive–behavioural therapy (CBT) only, without imputed studies; (c) all psychotherapy studies, with imputed studies (black circles); (d) CBT studies only, with imputed studies. Imputation according to Duval & Tweedie trim and fill procedure.
**Effect sizes of CBT: flatlining or falling?**

Figure 4. The plot portrays the negative change ($p < .001$) in Beck Depression Inventory effect sizes across time ($k = 61$). The size of the circles indicates the relative contribution (random weight) of each study to the analysis.

Effect sizes of CBT: flatlining/falling?

**Figure 6.** The plot portrays the negative change ($p = .03$) in the remission rates across time ($k = 42$). The size of the circles indicates the relative contribution (random weight) of each study to the analysis.

Effect sizes in comparative studies of psychotherapy for BPD decrease by year of publication

*Spearman rho = -0.468, p<.01*


Evidence-based treatments in young people
The “Dodo Bird Verdict”

All *bona fide* treatments are equally efficacious for *children and adolescents* with depression, anxiety, conduct disorder and ADHD

(pooled effect sizes after randomly assigning negative values = 0)

Benish et al, 2008; Imel et al., 2008; Miller et al., 2008; Spielmans et al., 2007
Effect sizes of interventions in youth: Five decades of research

- Multilevel meta-analysis: multiple outcomes
- N=447 studies, totaling 30,431 youths
- No evidence of publication bias
- No significant differences among treatment approaches = dodo bird verdict

Target problem was the most important moderator of treatment benefit

- Better outcome: less ‘co-morbidity’
- Not qualified by treatment type or control condition
- With regard to depression:
  - ES=.22 at follow-up = only about 60% are better off than control condition
- With regard to multiple problems
  - ES=.02 at follow-up = not better than no treatment
So where does this leave us?

- Most YP with depression in clinical practice present with ‘multiple problems’!
- Dearth of studies on ‘multiple problems’
  - n=10 in the Weisz et al. 2017 meta-analysis
  - Example: Recent review found only very few trials on treatment of BPD in adolescence (Fonagy et al., 2015)

THE IMPACT STUDY
Improving Mood With Psychoanalytic Psychotherapy And Cognitive Behaviour Therapy:

- Largest RCT of pediatric depression so far
- $N=465$ ITT, randomized to
  - Brief Psychosocial Intervention
  - CBT
  - PDT

However…

- A substantial proportion of patients (approximately 25%) continued to meet diagnostic criteria for unipolar major depression by 86 weeks.

- A further 15% reported depressive symptoms higher than the cut-off score (>26) for potential cases.

- Only 285 (60%) of the sample were available for full clinical assessment.

- Treatment resistance or non-compliance in this cohort overall is relatively high
‘Hard-to-reach’?

Number of therapy sessions attended

<table>
<thead>
<tr>
<th></th>
<th>BPI</th>
<th>CBT</th>
<th>STPP</th>
</tr>
</thead>
<tbody>
<tr>
<td>Median (IQR)</td>
<td>6 (4,11)</td>
<td>9 (5,14)</td>
<td>11 (5,23)</td>
</tr>
<tr>
<td>Planned</td>
<td>12</td>
<td>20</td>
<td>28</td>
</tr>
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</table>
“Flatlining of ESs over time might suggest a need to rethink the very research strategy through which psychological therapies for youths have been developed across five decades” (Weisz et al., 2017, p. 95)
Is that all there is? Have we reached a ceiling

Or, lo and behold, placebo?
So where does this lead us...?
New Directions

- A general psychopathology or ‘p’-factor
- An evolutionary informed view on salutogenesis
- The Research Domain Operating Criteria Initiative (RDoC)
The structure of psychopathology and the p-factor

- "Disorders" in psychiatry are highly comorbid
- Particular depression and anxiety: very high ‘co-morbidity’
- P-factor?: one general psychopathology factor that explains
  - Comorbidity among disorders
  - "Change" of disorder over time

The Bi-Factor Model:
The general psychopathology factor

Factor ‘P’

Syndrome level

Spectral level

The general psychopathology factor

Caspi et al., 2013 The p Factor One General Psychopathology Factor in the Structure of Psychiatric Disorders?

Clinical Psychological Science
The \( p \) factor appears to capture an underlying propensity for any kind of psychopathology.

- **Replicated across numerous samples**
  - **Children** ([Lahey et al., 2015; Murray, Eisner, & Ribeaud, 2016](#)),
  - **Adolescents** ([Blanco et al., 2015; Carragher et al., 2016; Laceulle, Nederhof, van Aken, & Ormel, 2015; Lahey et al., 2012; Murray et al., 2016; Noordhof, Krueger, Ormel, Oldehinkel, & Hartman, 2015; Patalay et al., 2015; Tackett et al., 2013](#)),
  - **Adults** ([Caspi et al., 2014; Lahey et al., 2012](#)),
<table>
<thead>
<tr>
<th>Predictor</th>
<th>B</th>
<th>Wald</th>
<th>Odds-ratio</th>
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</thead>
<tbody>
<tr>
<td>Patalay, Fonagy et al. 2015</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Br J Psychiatry community-based sample</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><em>aged 11-14 years (N= 23, 477)</em></td>
<td></td>
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<tr>
<td><strong>2-factor model</strong></td>
<td></td>
<td></td>
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</tr>
<tr>
<td>Internalising</td>
<td>.49***</td>
<td>76.4</td>
<td>1.80</td>
</tr>
<tr>
<td>Externalising</td>
<td>1.41***</td>
<td>689.64</td>
<td>4.11</td>
</tr>
<tr>
<td><strong>Bi-factor model</strong></td>
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<td></td>
<td></td>
</tr>
<tr>
<td>Internalising</td>
<td>.22</td>
<td>4.43</td>
<td>1.25</td>
</tr>
<tr>
<td>Externalising</td>
<td>1.43***</td>
<td>413.74</td>
<td>4.16</td>
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<tr>
<td>P-Factor</td>
<td>2.33***</td>
<td>479.01</td>
<td>10.30</td>
</tr>
</tbody>
</table>
The ‘P’ Factor (Caspi et al., 2013)

Ungendered chronic Psychotic conditions

Partially gendered Personality disorder

Gendered Neurotic’ conditions

Male Gender Style

Female

Persistence

Impairment

Externalizing Internalizing


Elephant in the room

“I’m right there in the room, and no one even acknowledges me.”
An evolutionary-based social cognition or communication-based approach to personality disorder
Brains and social behavior vary across different mammalian species

- **Insectivors**: Regulated maternal behaviors

- **Chimpanzees**: Societies of a **few dozen**

- **Modern Humans**: Societies of **millions** of interacting people

Humans exceedingly skilled at **large scale social interaction**

**Competition for social skills** led to the evolutions of cognitive **mechanism for collaborating** with others

Fuelled **evolution of human brain**.

*Therefore correlation in mammals between size of social group and volume of neocortex*
Species-specific ways to acquire beliefs

- We can accept a culturally transmitted belief for **two reasons** (Sperber, 1997, 2001, Sperber et al., 2010)
  - To accept because of **content**: deductive reasoning
  - To accept on account of the **authority** (‘deferentially’ transmitted, Recanati, 1997)
    - The **source** is **known**, **remembered** and **judged** to be reliable (or trustworthy)
    - First in attachment relationships: **need to feel validated and understood** first **BEFORE** epistemic trust can be developed
Or give it to your mother.
She knows how to do it.
Figure 1. The Stress–Reward–Mentalizing (SRM) Model of Depression.

**Behavior**
- Stress sensitivity ↑
- Stress generation ↑

**Circuits and physiology**
- Stress system
  - Allostatic load
- Reward system
  - Imbalance in mesolimbic–mesocortical circuits
- Mentalizing system
  - Imbalance in cognitive/controlled–affective/automatic mentalizing

**Genes**
- e.g. 5HT, BDNF, COMT
- e.g., DRD1, OXTR, AVPR1A, MOR
- e.g., 5HTT, OXTR, COMT, ?

Major developmental challenges

- Relationship difficulties (e.g., social loss, rejection)
- Problems with agency/autonomy (e.g., failure, loss of social status)

Structural and functional reorganization of neural circuits involved in reward and mentalizing in adolescence

Stress

- +

Secondary attachment strategies

- +


Domains in childhood/adolescent depression

• To what extent do current treatments address the main **core domains** in youth depression?
  • Treatment are typically **underspecified**

• There is a need for a more **integrative treatment** approach that may **flexibly address** the different core domains in youth depression

Treatment Implications
We may need to change first in order to be able to improve our ability to change depressed youth

- **HOW** we offer treatment
- **WHERE** we offer treatment
HOW we offer treatment
Three types of youth with depression?

- Attachment relationships
  - Epistemic hypervigilance
  - Epistemic mistrust
  - Epistemic trust

- Development of epistemic trust needed
- Social learning can be reactivated
- Social learning can be used
WHERE we offer treatments
Building a social network begins early
When the capacity to form bonds of trust is shaky and tends to break down…
…we lose our safety net
Reconceptualising understanding not in terms of disease mechanisms...
...but as an absence of epistemic trust...
...which may once have been adaptive
Traditional therapeutic model

Patient and therapist are isolated in a room
But the reality is that the therapist becomes part of the patient’s (dysfunctional) social system, and systemic intervention may be required to address this
The therapist requires their own system of support relationships with other clinicians in order to scaffold their capacity to mentalize and facilitate epistemic trust.
Conclusions

- We may have hit the ceiling with treatments for youth depression

- **However**: recent developments suggest we may improve treatments by:
  - **Tailoring treatment** to youth with depression both in terms of **types of domains** affected and **general severity** or ‘p-’factor
  - This includes **leaving the secure base** of our office and **our ways of thinking** about young people with troubled minds
For more information:

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