Bipolar disorder, sleep and cognition

Peter Gallagher
Lecturer in Neuropsychology

Institute of Neuroscience & Newcastle University Institute for Ageing

Mood disorders research – a global effort …

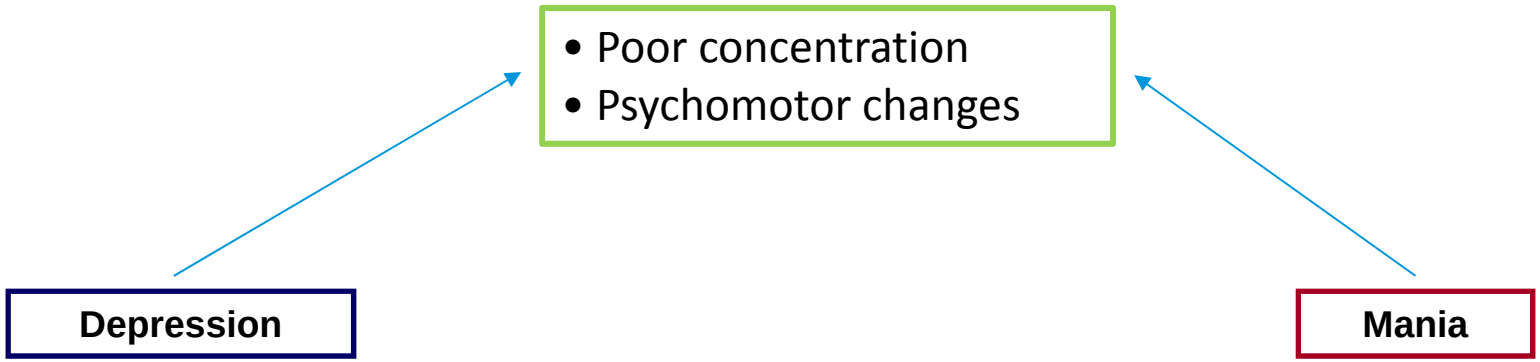
Mood disorders research – a global effort …

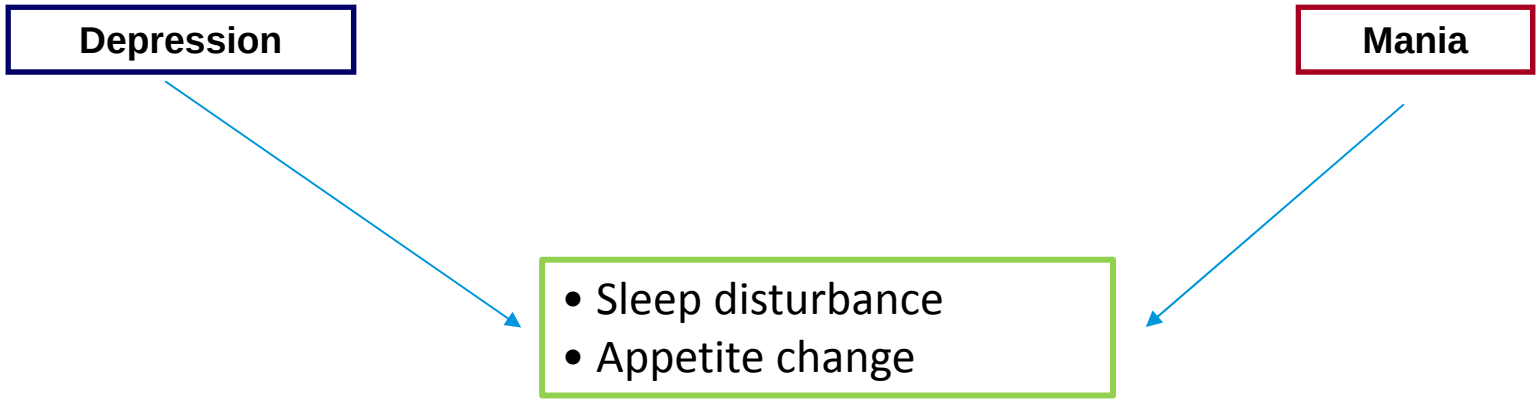
Depression

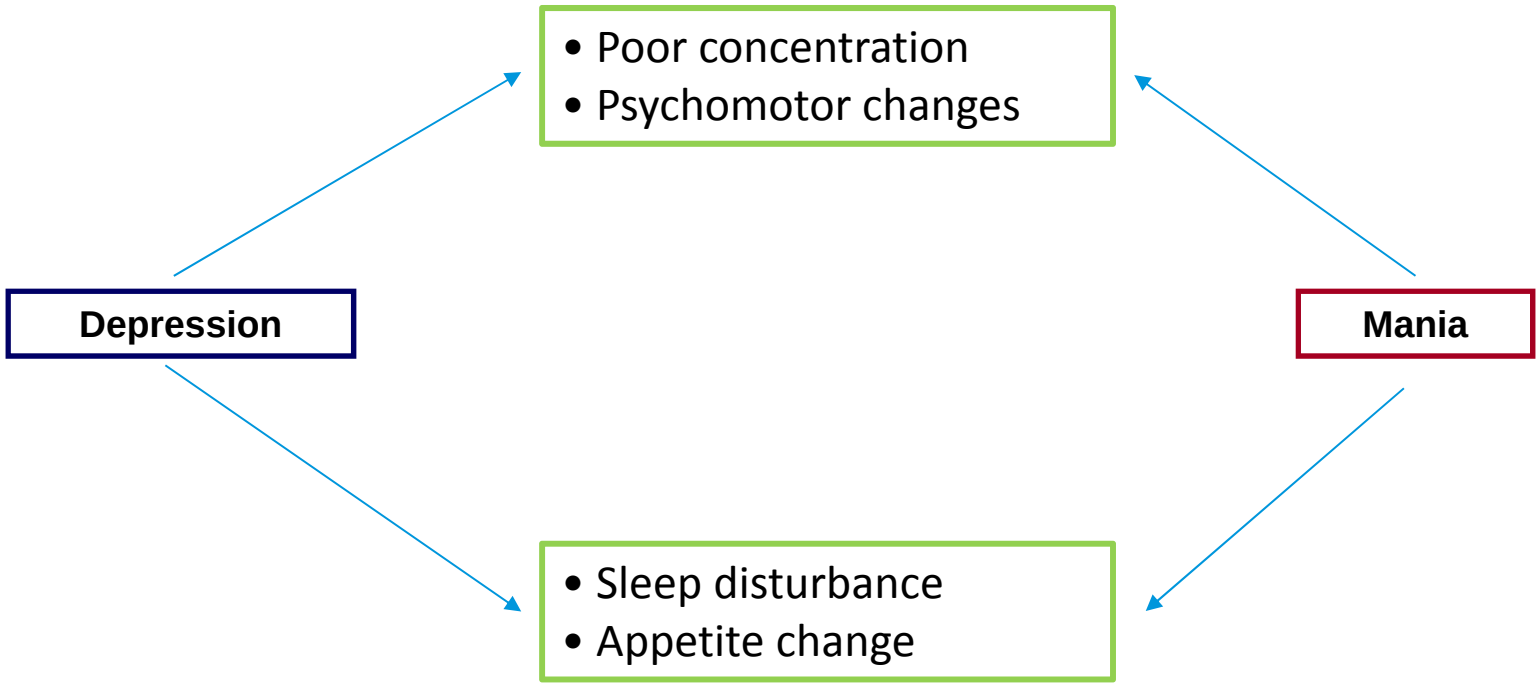
- Low mood
- Guilt, worthlessness
- Fatigue, low energy
- Anhedonia
- Suicidal ideas/thoughts

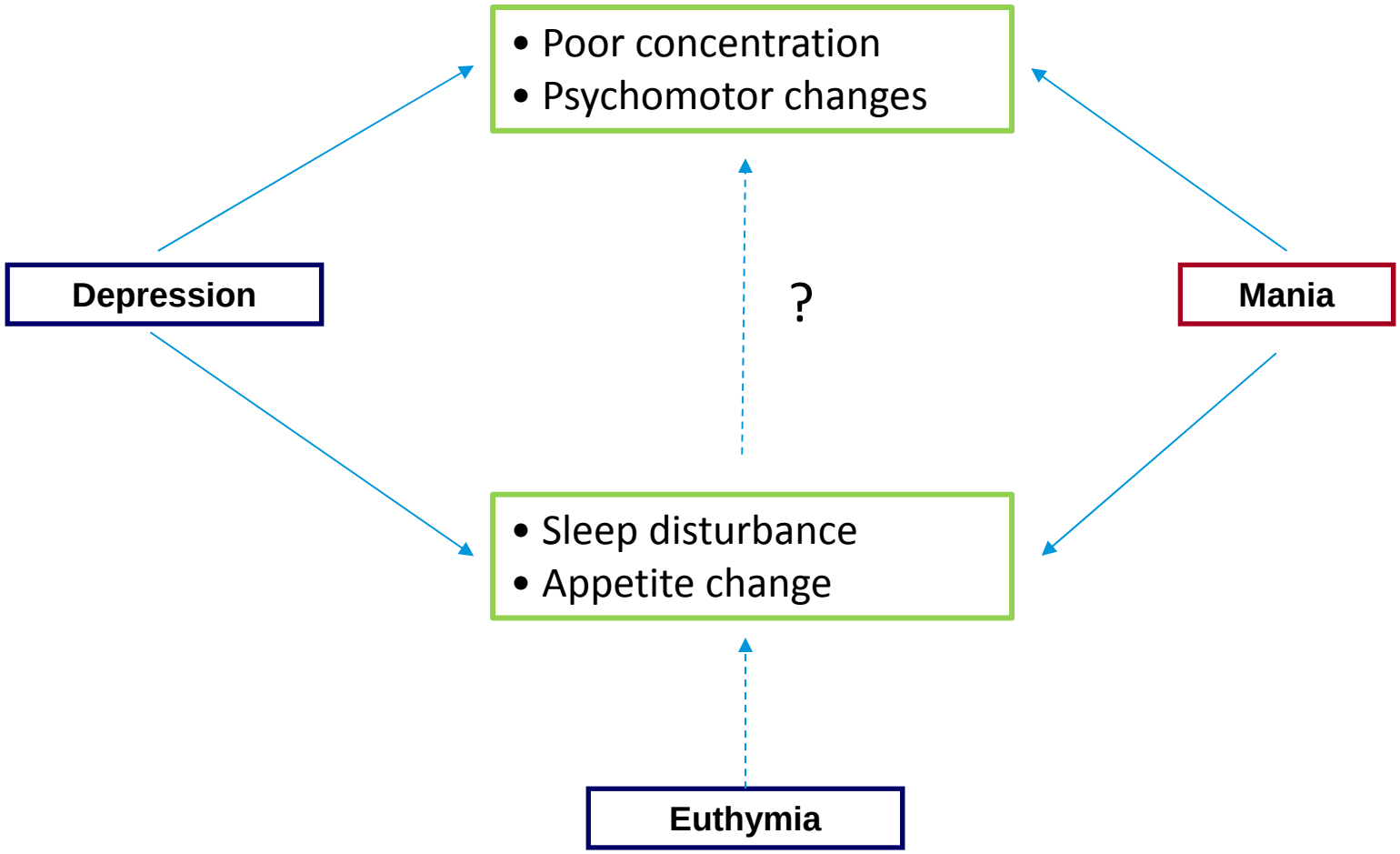
Mania

- Elevated mood
- Grandiosity
- Distractibility
- Talkativeness
- Racing thoughts


• Poor concentration
• Psychomotor changes
Depression
Mania


Depression
Mania
• Sleep disturbance
• Appetite change


• Poor concentration
• Psychomotor changes
Depression
Mania
• Sleep disturbance
• Appetite change


• Poor concentration
• Psychomotor changes
Depression
?
Mania
• Sleep disturbance
• Appetite change
Euthymia

Cognitive impairment in BD – group level

BRITISH JOURNAL OF PSYCHIATRY (2005), 186, 32–40

Neurocognitive impairment in euthymic patients with bipolar affective disorder

JILL M. THOMPSON, PETER GALLAGHER, JOHN H. HUGHES, STUART WATSON, JOHN M. GRAY, I. NICOL FERRIER and ALLAN H. YOUNG

- N=126 (63 euthymic BD, 63controls)

Psychological Medicine (2014), **44**, 961–974.
doi:10.1017/S0033291713001487

ORIGINAL ARTICLE

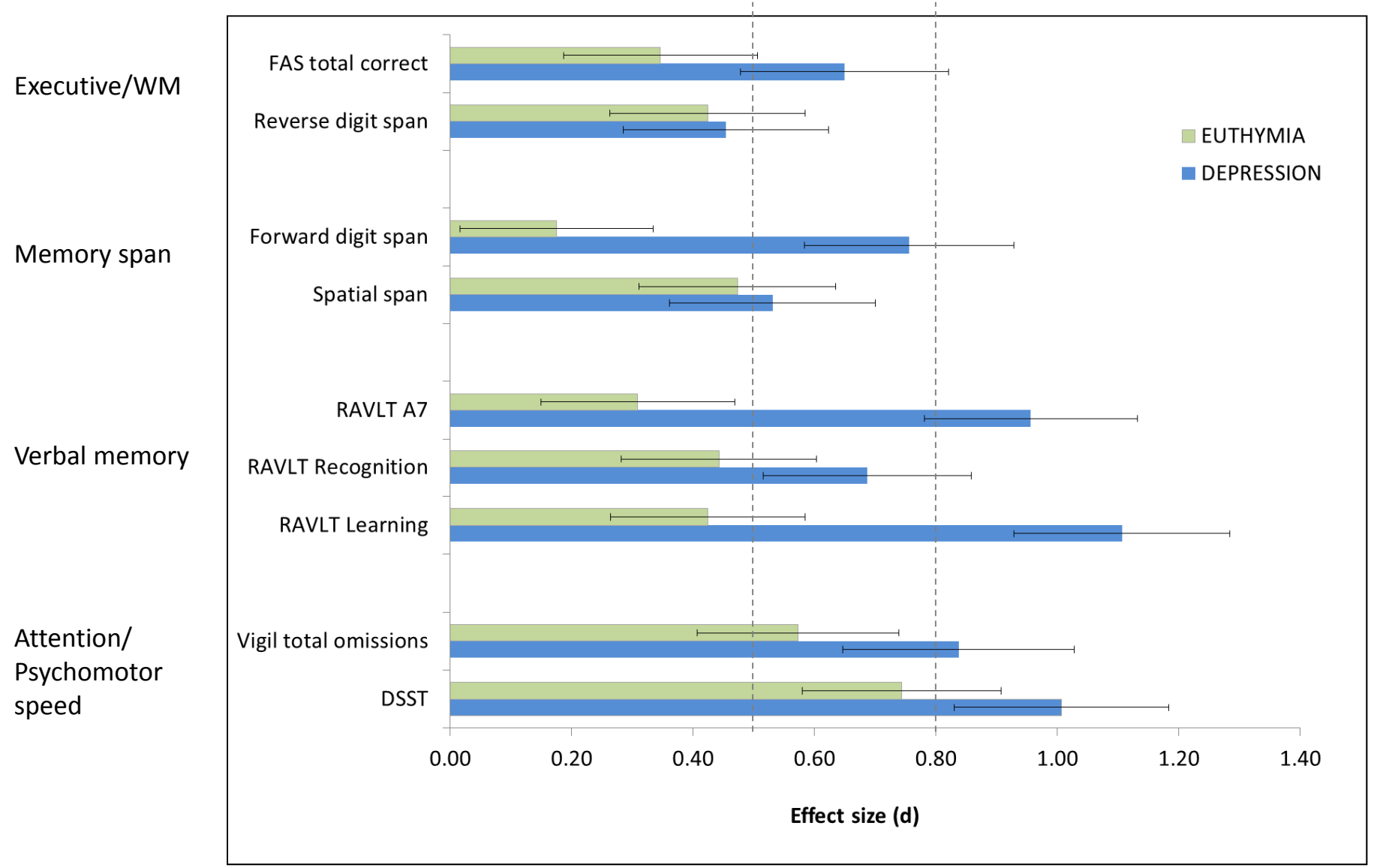
Neurocognitive functioning in bipolar depression: a component structure analysis

P. Gallagher[1]*, J. M. Gray[1], S. Watson[1], A. H. Young[2] and I. N. Ferrier[1]

[1] *Institute of Neuroscience (Academic Psychiatry), Newcastle University, UK*
[2] *Centre for Mental Health, Imperial College London, UK*

- N=100 (53 depressed BD, 47 controls)

Cognitive profile - euthymia *vs.* depression



Pooled data from: - Thompson JM, Gallagher P, Hughes JH, Watson S, Gray JM, Ferrier IN, Young AH (2005). *British Journal of Psychiatry* 186, 32-40
- Gallagher P, Gray JM, Watson S, Young AH, Ferrier IN (2014). *Psychological Medicine* 44, 961–974.

Cognitive function – defining 'impairment'

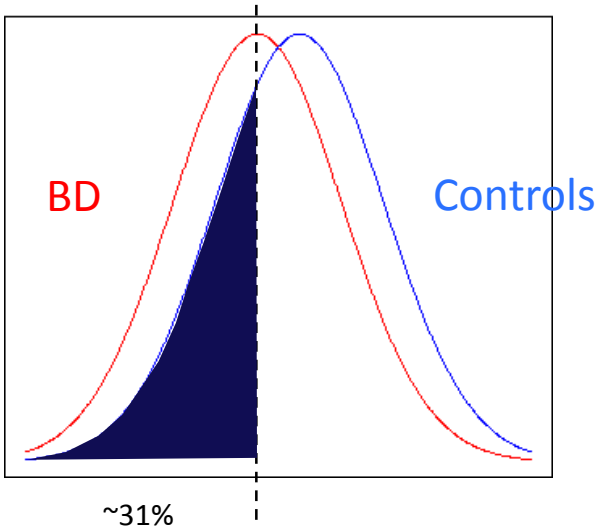
z	Percentile standing	d	Cohen's U_1	*Non-overlap (%)	*Overlap (%)
0.0	50.0	**0.0**	0.0	0.0	100.0
-0.1	46.0	**0.1**	7.7	4.0	96.0
-0.2	42.0	**0.2**	14.7	8.0	92.0
-0.3	38.0	**0.3**	21.3	11.9	88.1
-0.4	34.0	**0.4**	27.4	15.8	84.2
-0.5	31.0	**0.5**	33.4	19.7	80.3
-0.6	27.0	**0.6**	38.2	23.6	76.4
-0.7	24.0	**0.7**	43.0	27.4	72.6
-0.8	21.0	**0.8**	47.4	31.1	68.9
-0.9	18.0	**0.9**	51.6	34.7	65.3
-1.0	16.0	**1.0**	55.4	38.3	61.7
-1.1	14.0	**1.1**	58.9	41.8	58.2
-1.2	12.0	**1.2**	62.2	45.2	54.8
-1.3	10.0	**1.3**	65.3	48.4	51.6
-1.4	8.1	**1.4**	68.1	51.6	48.4
-1.5	6.7	**1.5**	70.7	54.7	45.3
-1.6	5.5	**1.6**	73.1	57.6	42.4
-3.0	0.1	**3.0**	92.8	86.6	13.4
-3.2	<0.1	**3.2**	94.2	89.0	11.0
-3.4	<0.1	**3.4**	95.3	91.1	8.9
-3.6	<0.1	**3.6**	96.3	92.8	7.2
-3.8	<0.1	**3.8**	97.0	94.3	5.7
-4.0	<0.1	**4.0**	97.7	95.5	4.5

← 'small'

← 'medium'

← 'large'

Normal distributions with d=0.5



* Grice, J. W., & Barrett, P. T. (2011). *A note on Cohen's overlapping proportions of normal distributions*. Stillwater, OK: Oklahoma State University, Dept. of Psychology.

McGough, J. J. & Faraone, S. V. (2009). Estimating the size of treatment effects: moving beyond p values. *Psychiatry, 6(10),* 21-9.

Zakzanis, K. K. (2001). Statistics to tell the truth, the whole truth, and nothing but the truth: Formulae, illustrative numerical examples, and heuristic interpretation of effect size analyses for neuropsychological researchers. *Archives of Clinical Neuropsychology, 16*(7), 653-667.

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DOI: 10.1111/bdi.12602

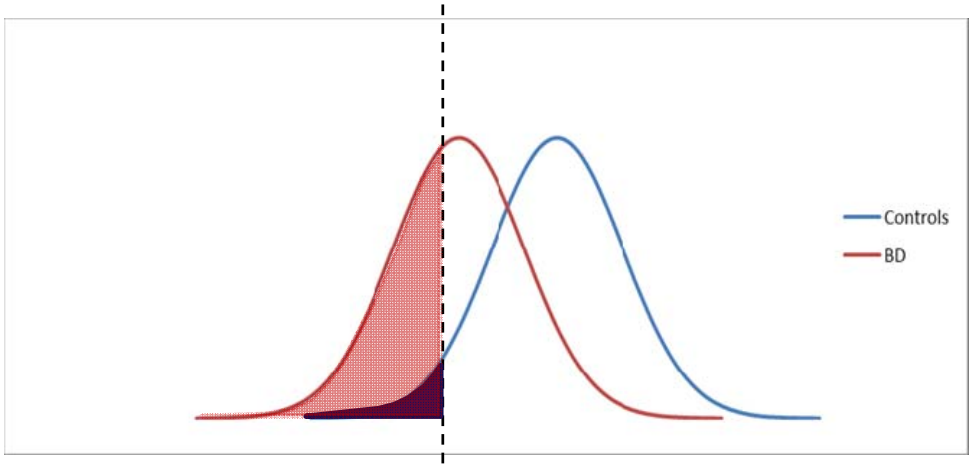
ORIGINAL ARTICLE

WILEY BIPOLAR DISORDERS

Prevalence of cognitive impairment in major depression and bipolar disorder

Katie M Douglas[1] | Peter Gallagher[2] | Lucy J Robinson[2] | Janet D Carter[3] | Virginia VW McIntosh[3] | Christopher MA Frampton[1] | Stuart Watson[2] | Allan H Young[4,5] | I Nicol Ferrier[2] | Richard J Porter[1,6]

- For each test, z-scores calculated based on mean and SD of controls
- Cognitive variables then grouped to fit into one of four cognitive domains:
  - (i) verbal learning & memory
  - (ii) visuospatial learning & memory
  - (iii) executive function/attention
  - (iv) psychomotor speed
- Impairment was defined as the proportion of subjects performing at or below predefined cut-offs



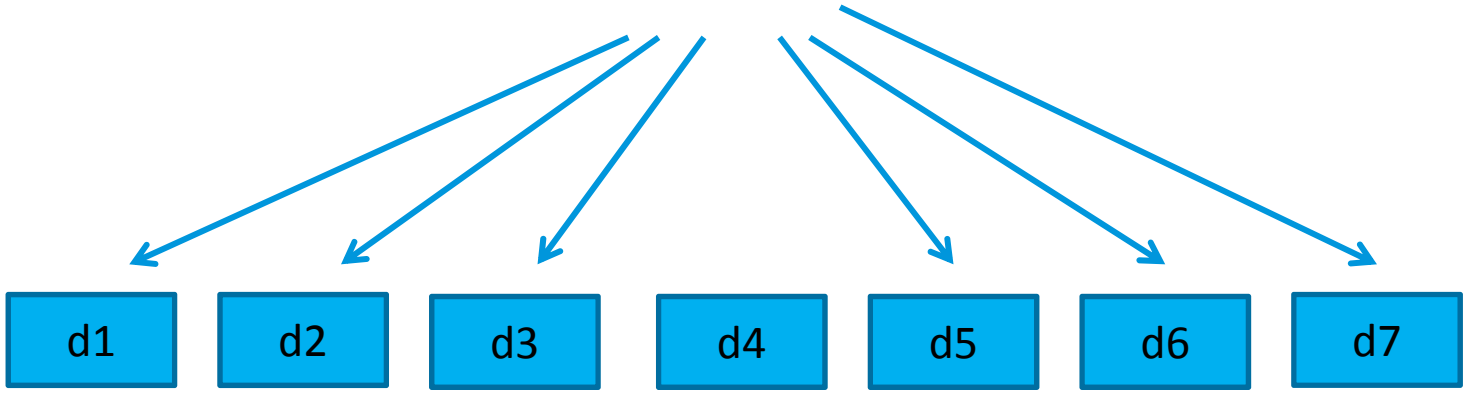
≤ 1.5 SD (~7th percentile) cut-off

TABLE 4 Prevalence (%) of impairment using four approaches to classify cognitive impairment

	Study 3 Bipolar depression		Study 4 Euthymic bipolar	
	Patient	Control	Patient	Control
Cognitive domains: number of domains impaired				
1.5 SD				
No domains impaired	53.5	86.8	61.9	93.6
≥1 domains impaired	46.5	13.2	38.1	6.4
≥2 domains impaired	17.9	1.9	20.6	1.6
≥3 domains impaired	5.4	0.0	11.1	0.0

≥ 1.5 SD	Bipolar Depression		Euthymic bipolar	
	Patient	Control	Patient	Control
Verbal learning and memory	23.2	3.8	12.7	3.2
Visual spatial learning and memory	17.9	3.8	15.9	3.2
Executive function	5.4	0.0	14.3	1.6
Psychomotor speed	23.2	7.5	29.0	1.6

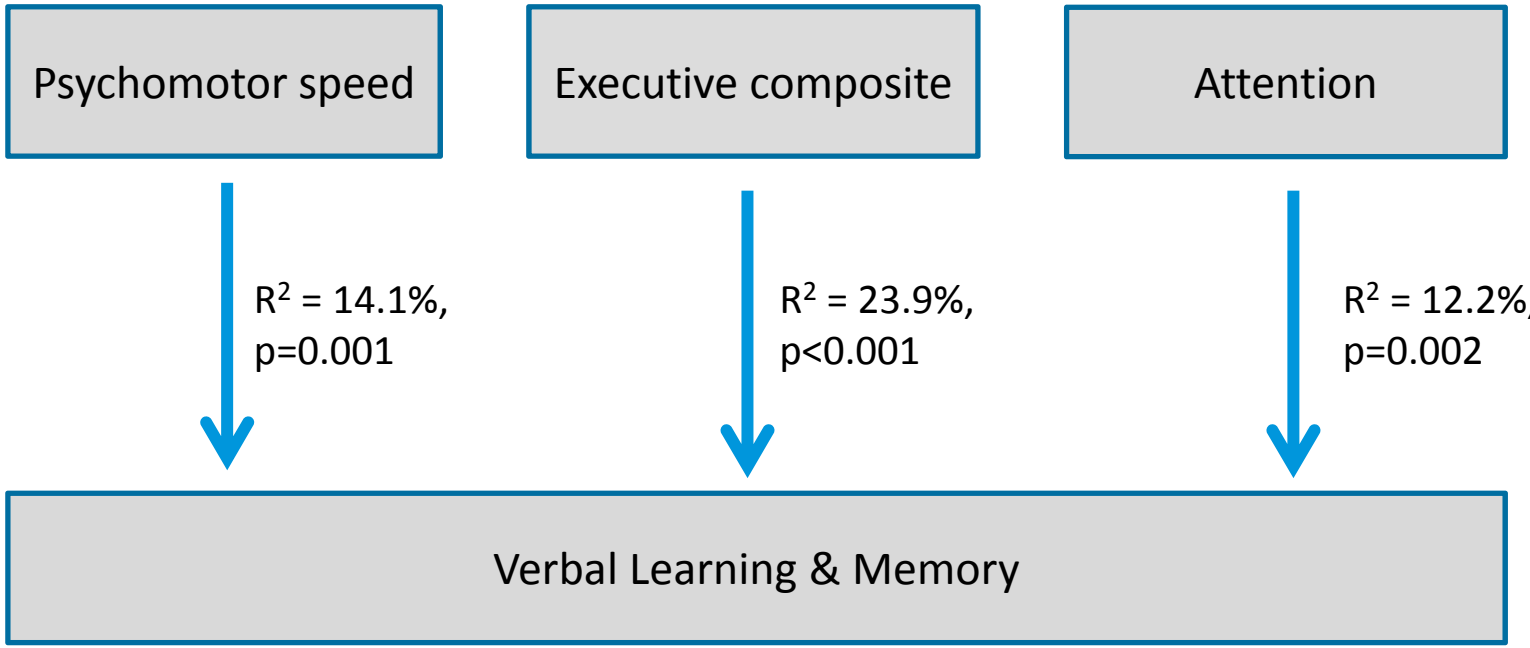
Cognitive hierarchy of mood disorder



Psychomotor speed / Attention

Cognitive hierarchy in bipolar disorder

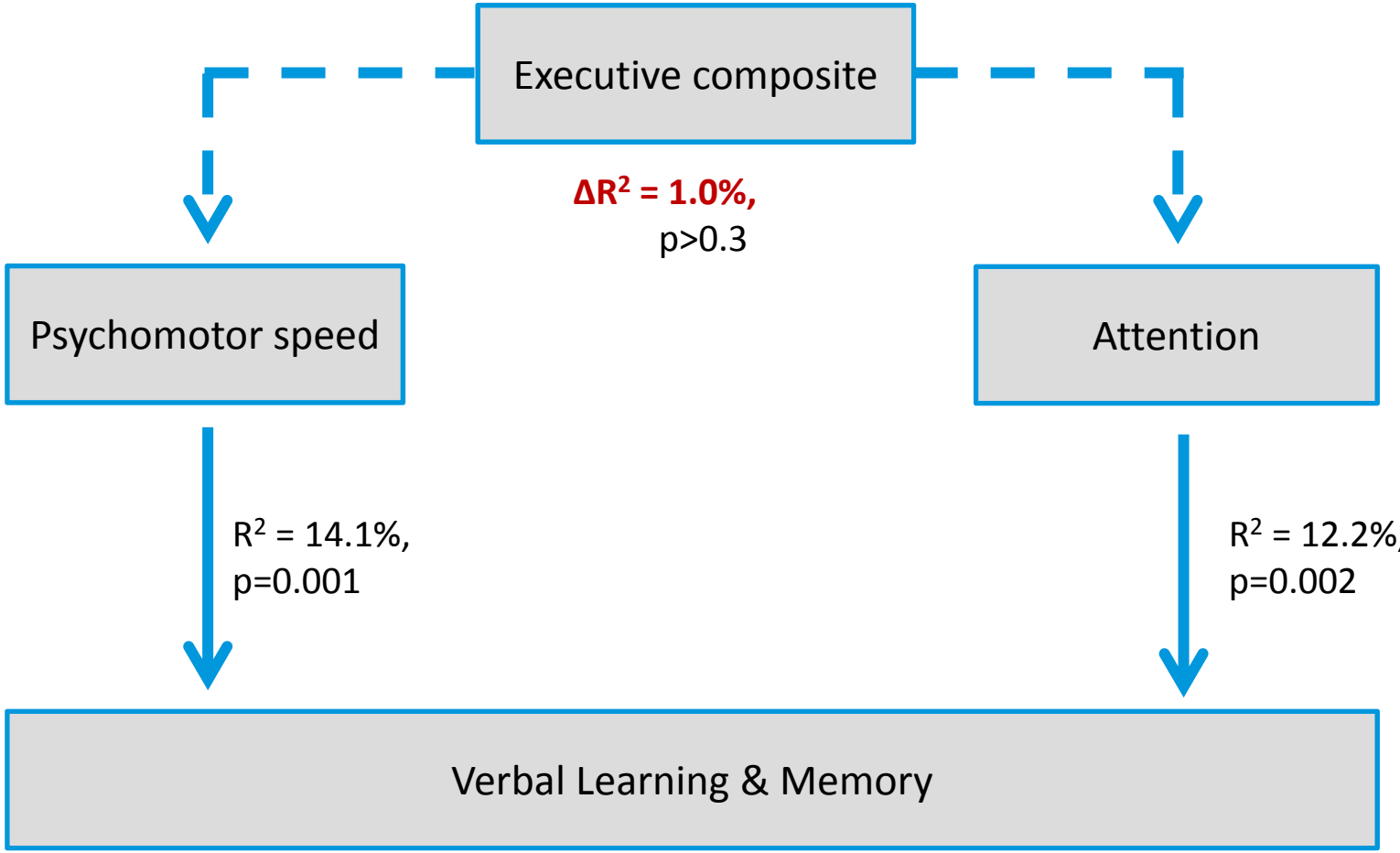
depression



n=43 bipolar depressed, n=32 controls

Cognitive hierarchy in bipolar disorder

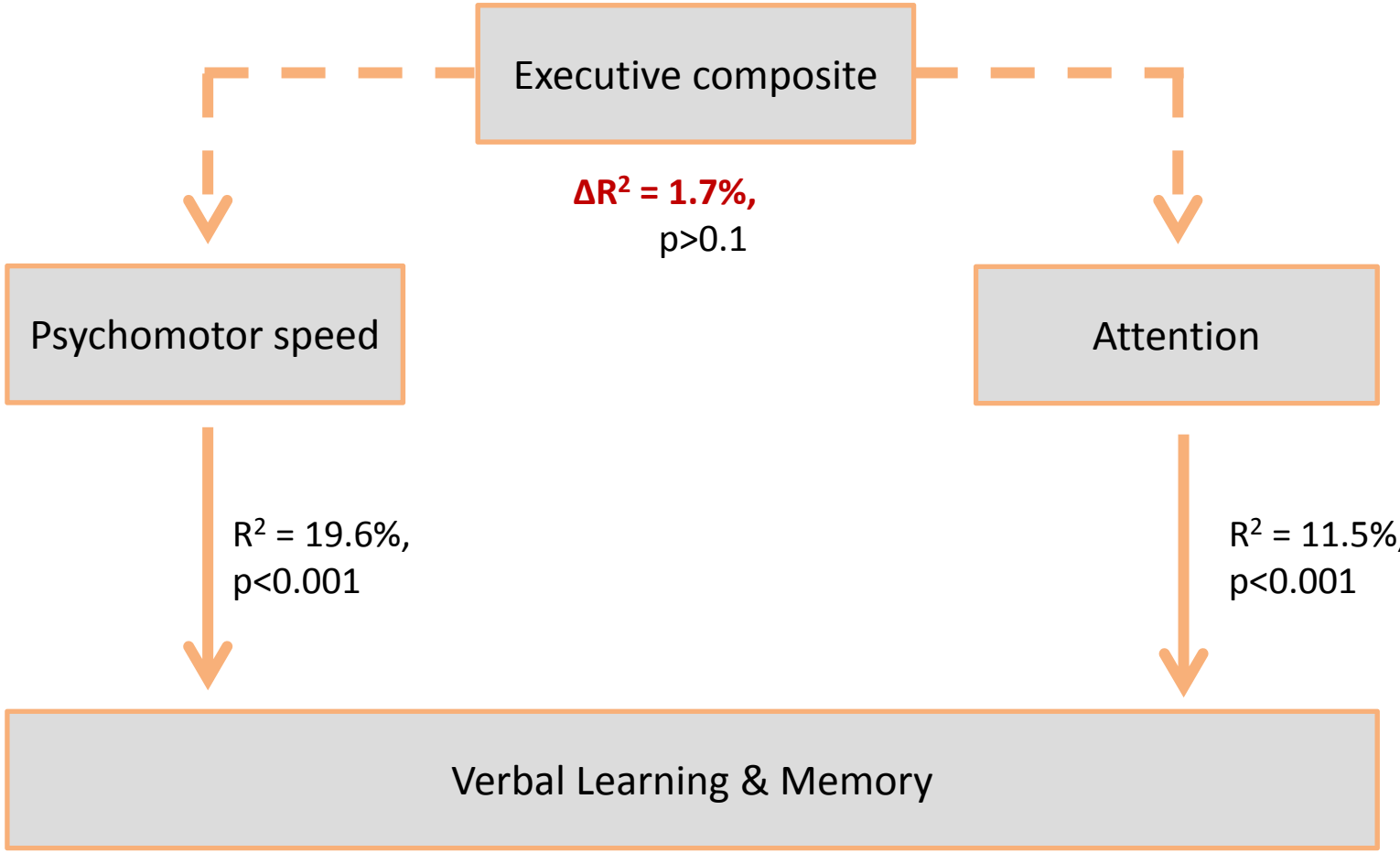
depression



n=43 bipolar depressed, n=32 controls

Cognitive hierarchy in bipolar disorder

euthymia

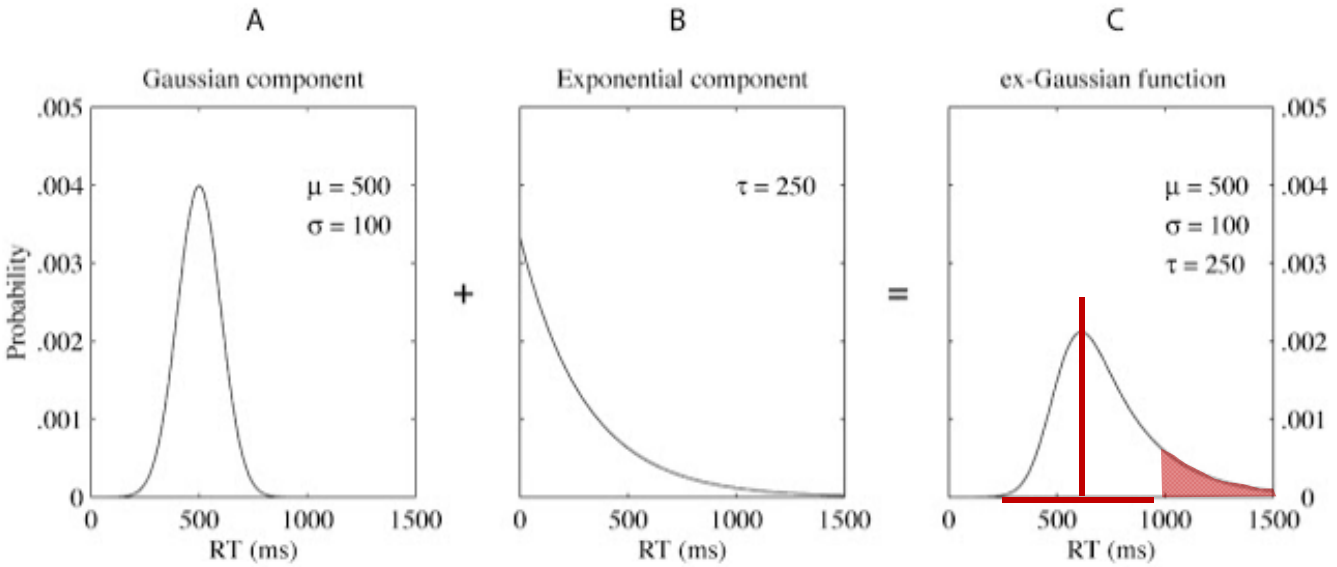


n=63 bipolar euthymic, n=62 controls

Cognitive intra-individual variability

- Does ex-Gaussian modelling improve discrimination of attentional RT measures in mood disorder?

Lacouture 2008



- Mu and sigma: mean and sd of the Gaussian (normal) component

- Tau: the 'slow tail' of the distribution

Cognitive intra-individual variability

Psychological Medicine (2015), **45**, 2985–2997. © Cambridge University Press 2015
doi:10.1017/S0033291715000926

ORIGINAL ARTICLE

Neurocognitive intra-individual variability in mood disorders: effects on attentional response time distributions

P. Gallagher[1*], J. Nilsson[1,2], A. Finkelmeyer[1], M. Goshawk[1], K. A. Macritchie[3], A. J. Lloyd[1,4], J. M. Thompson[1], R. J. Porter[5], A. H. Young[6], I. N. Ferrier[1], R. H. McAllister-Williams[1,4] and S. Watson[1,4]

- Vigil Continuous Performance Test
  - 8 minute sustained test (requiring 100 target responses)
  - Reaction time recorded for each target response.

- 138 healthy controls and 158 patients with a mood disorder
  - 86 euthymic BD, 33 depressed BD and 39 medication-free MDD patients.

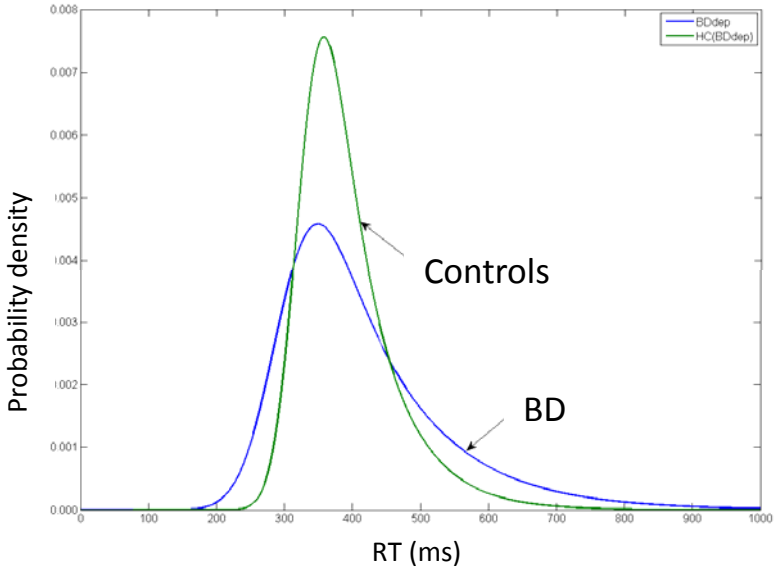
Cognitive variability – BD

depression

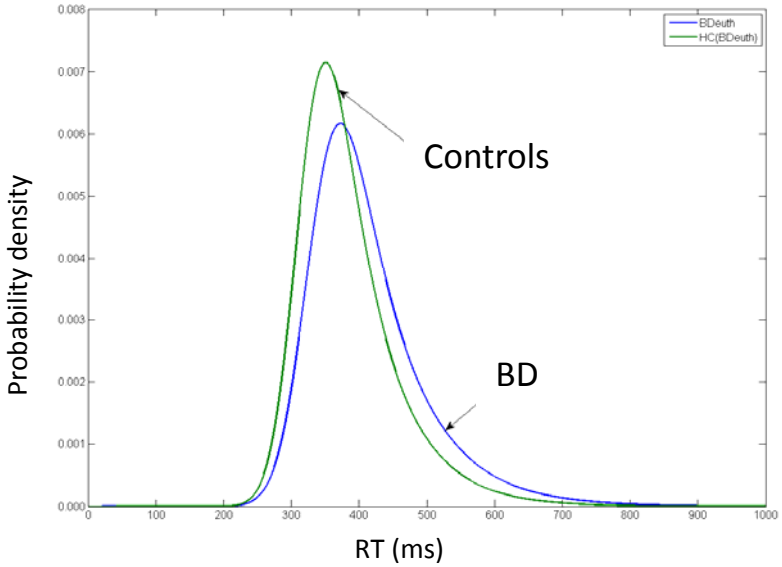
	BD depressed (n=33)		Control comparison (n=33)			
	Mean	SD	Mean	SD		
iSD	143.78	56.21	80.72	29.70	**$F_{1,64} = 32.47$**	**$p < 0.0001$**
Mu	295.98	87.66	324.63	82.76	$F_{1,64} = 1.86$	$p = 0.177$
Sigma	45.23	33.85	29.78	18.46	**$F_{1,64} = 5.29$**	**$p = 0.025$**
Tau	117.33	59.40	66.29	22.32	**$F_{1,64} = 21.35$**	**$p < 0.0001$**

euthymia

	BD euthymic (n=86)		Control comparison (n=86)			
	Mean	SD	Mean	SD		
iSD	95.85	29.93	85.43	33.34	**$F_{1,170} = 4.79$**	**$p = 0.030$**
Mu	332.17	76.55	315.96	75.93	$F_{1,170} = 1.94$	$p = 0.165$
Sigma	37.68	21.19	33.15	21.78	$F_{1,170} = 1.92$	$p = 0.168$
Tau	78.85	32.55	66.77	28.98	**$F_{1,170} = 6.60$**	**$p = 0.011$**

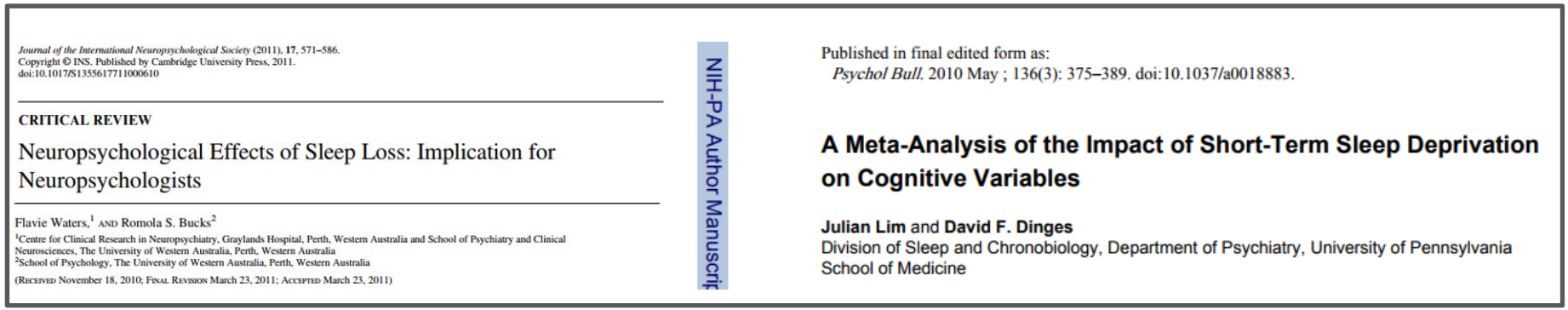


d= 1.14



d= 0.39

What is the effect of sleep disturbance on cognition?



Journal of the International Neuropsychological Society (2011), **17**, 571–586.

doi:10.1017/S1355617711000610

CRITICAL REVIEW

Neuropsychological Effects of Sleep Loss: Implication for Neuropsychologists

Flavie Waters,[1] AND Romola S. Bucks[2]
[1]Centre for Clinical Research in Neuropsychiatry, Graylands Hospital, Perth, Western Australia and School of Psychiatry and Clinical Neurosciences, The University of Western Australia, Perth, Western Australia
[2]School of Psychology, The University of Western Australia, Perth, Western Australia
(RECEIVED November 18, 2010; FINAL REVISION March 23, 2011; ACCEPTED March 23, 2011)

Published in final edited form as:
Psychol Bull. 2010 May ; 136(3): 375–389. doi:10.1037/a0018883.

A Meta-Analysis of the Impact of Short-Term Sleep Deprivation on Cognitive Variables

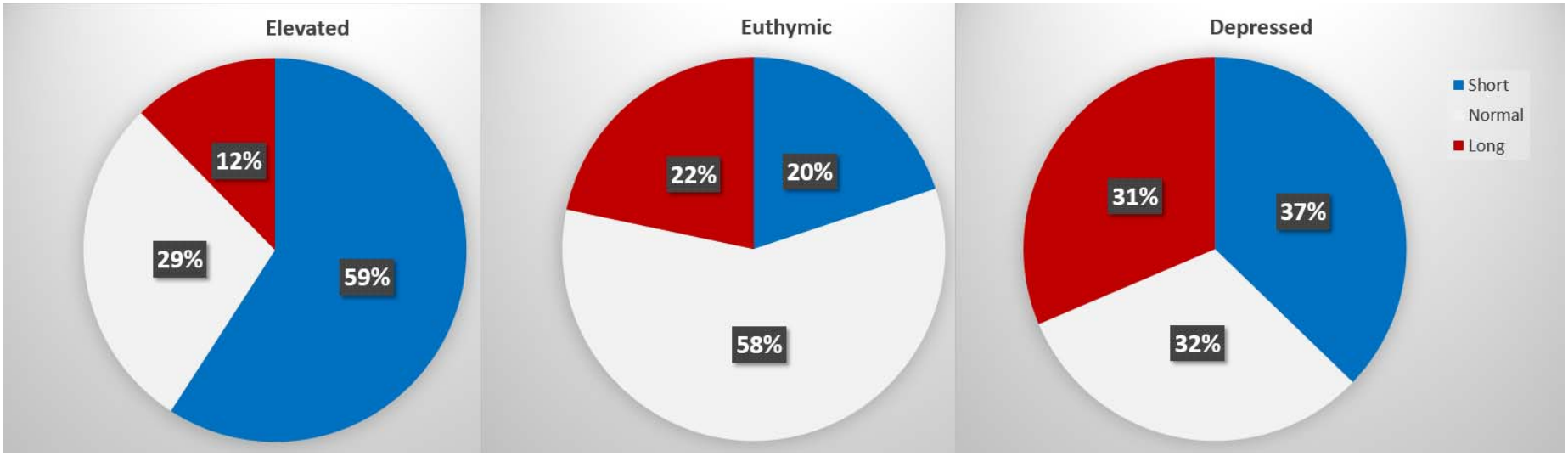
Julian Lim and **David F. Dinges**
Division of Sleep and Chronobiology, Department of Psychiatry, University of Pennsylvania School of Medicine

- Sleep disturbance impacts on multiple aspects of cognition.
  - The effect sizes of the impact of sleep loss on cognitive deficits are in the **"**moderate range**"** (Lim & Dinges, 2010), with the largest effect size on tasks of processing speed and attention/vigilance.
  - *Milder, and less consistent, deficits have been found in executive functions, mental arithmetic, short-term memory, memory and language.*

- The most reliable finding after sleep disturbance is that of decreased speed of processing.
  - Studies using speed as an outcome measure are more likely to report impairing effects from sleep loss than studies that report only accuracy data.

Sleep disturbance in bipolar disorder

- Sleep disturbance is a core symptom of bipolar disorder and is exhibited across mood phases.
- 2,024[a] individuals with bipolar disorder drawn from the STEP-BD study.
  - 641 participants (31.7 %) were classified as short sleepers (< 6 h)
  - 467 participants (23.1 %) as long sleepers (≥ 9 h)
  - 760 participants (37.5 %) as normal sleepers



Gruber, J., et al. (2009). Journal of Affective Disorders, 114, 41-49.

[a] *156 (7.7%) not-classified*

Psychological Medicine (2017), **47**, 1678–1689. © Cambridge University Press 2017
doi:10.1017/S0033291717000186

ORIGINAL ARTICLE

Sleep and circadian rhythm disturbance in bipolar disorder

A. J. Bradley[1,2], R. Webb-Mitchell[1], A. Hazu[1], N. Slater[1], B. Middleton[3], P. Gallagher[1], H. McAllister-Williams[1,4] and K. N. Anderson[5]*

[1] *Institute of Neuroscience, Newcastle University, Wolfson Research Centre, Campus for Aging and Vitality, Newcastle Upon Tyne, UK*
[2] *Eli Lilly and Company Limited, Lilly House, Basingstoke, UK*
[3] *Surrey Sleep Research Centre and Centre for Chronobiology, Faculty of Health and Medical Sciences, University of Surrey, Guildford, UK*
[4] *Northumberland, Tyne and Wear NHS Foundation Trust, Newcastle, UK*
[5] *Regional Sleep Service, Freeman Hospital, High Heaton, Newcastle upon Tyne, UK*

- 46 patients with BD and 42 controls
- Comprehensive sleep/circadian rhythm assessment:
  - respiratory sleep studies
  - prolonged accelerometry over 3 weeks
  - sleep questionnaires and diaries
  - melatonin levels
  - mood, psychosocial functioning and QoL

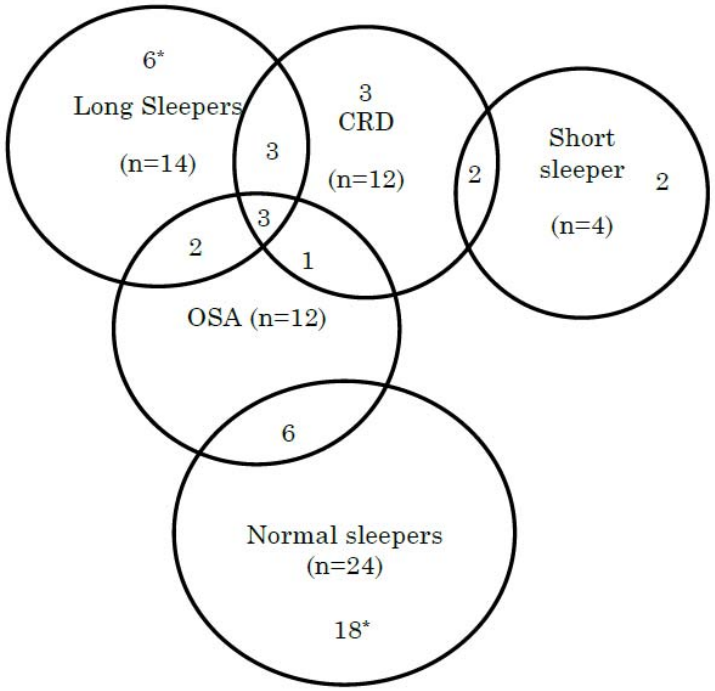
Psychological Medicine (2017), **47**, 1678–1689. © Cambridge University Press 2017
doi:10.1017/S0033291717000186

ORIGINAL ARTICLE

Sleep and circadian rhythm disturbance in bipolar disorder

A. J. Bradley[1,2], R. Webb-Mitchell[1], A. Hazu[1], N. Slater[1], B. Middleton[3], P. Gallagher[1], H. McAllister-Williams[1,4] and K. N. Anderson[5]*

[1] *Institute of Neuroscience, Newcastle University, Wolfson Research Centre, Campus for Aging and Vitality, Newcastle Upon Tyne, UK*
[2] *Eli Lilly and Company Limited, Lilly House, Basingstoke, UK*
[3] *Surrey Sleep Research Centre and Centre for Chronobiology, Faculty of Health and Medical Sciences, University of Surrey, Guildford, UK*
[4] *Northumberland, Tyne and Wear NHS Foundation Trust, Newcastle, UK*
[5] *Regional Sleep Service, Freeman Hospital, High Heaton, Newcastle upon Tyne, UK*



Normal sleepers = > 6 & < 10 hours nocturnal sleep and no CRD; Long sleepers = total 24 hour sleep > 10 hours; Short sleepers = nocturnal sleep < 6hours; CRD = circadian rhythm disorder; OSA = obstructive sleep apnoea.

- 50% of patients had abnormal sleep
- Associated with reduced 24h melatonin secretion (vs controls and normal sleepers)
- Abnormal sleep/CRD correlated with worse QoL.

Effects of sleep disturbance on cognition in BD

Attentional intra-individual variability

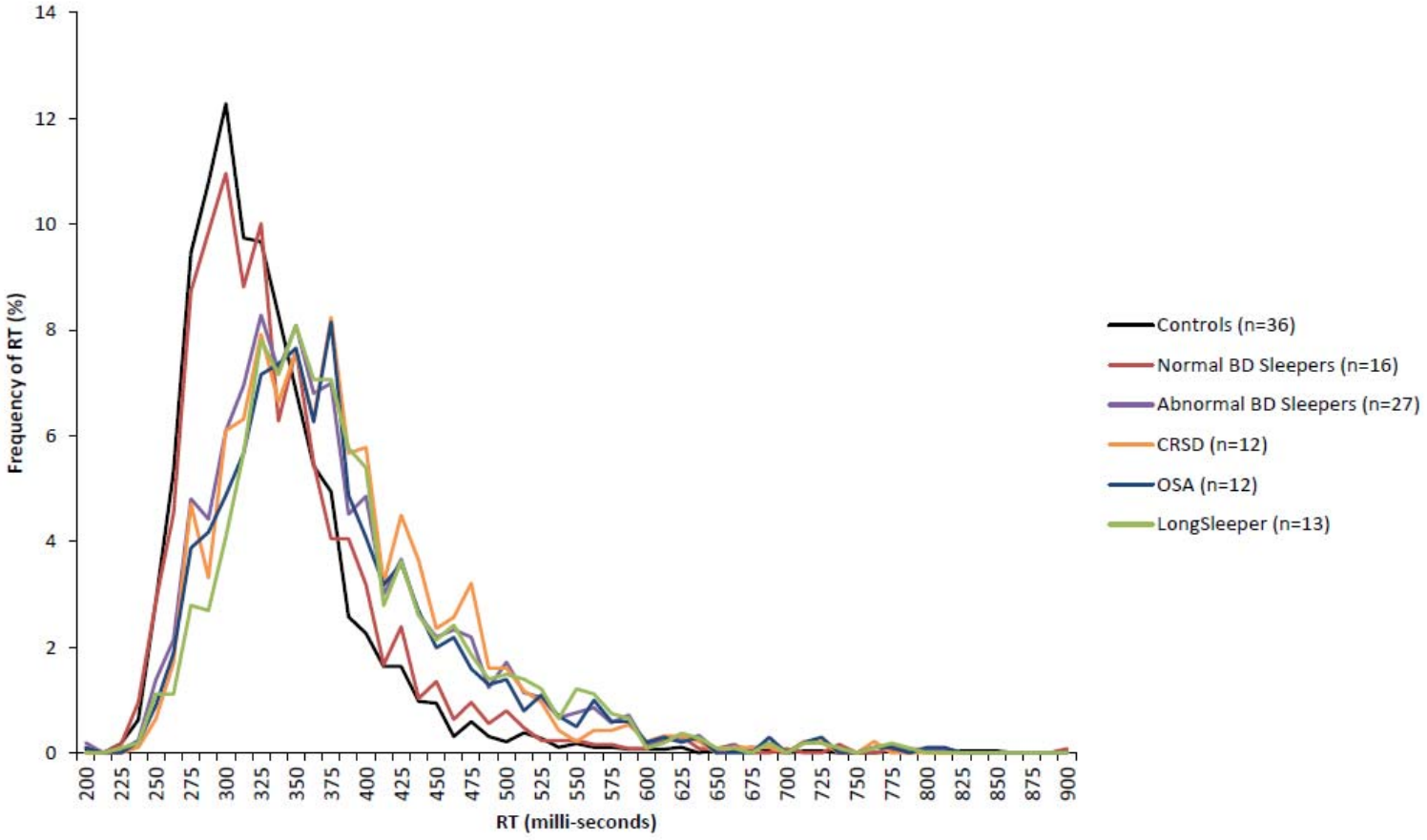
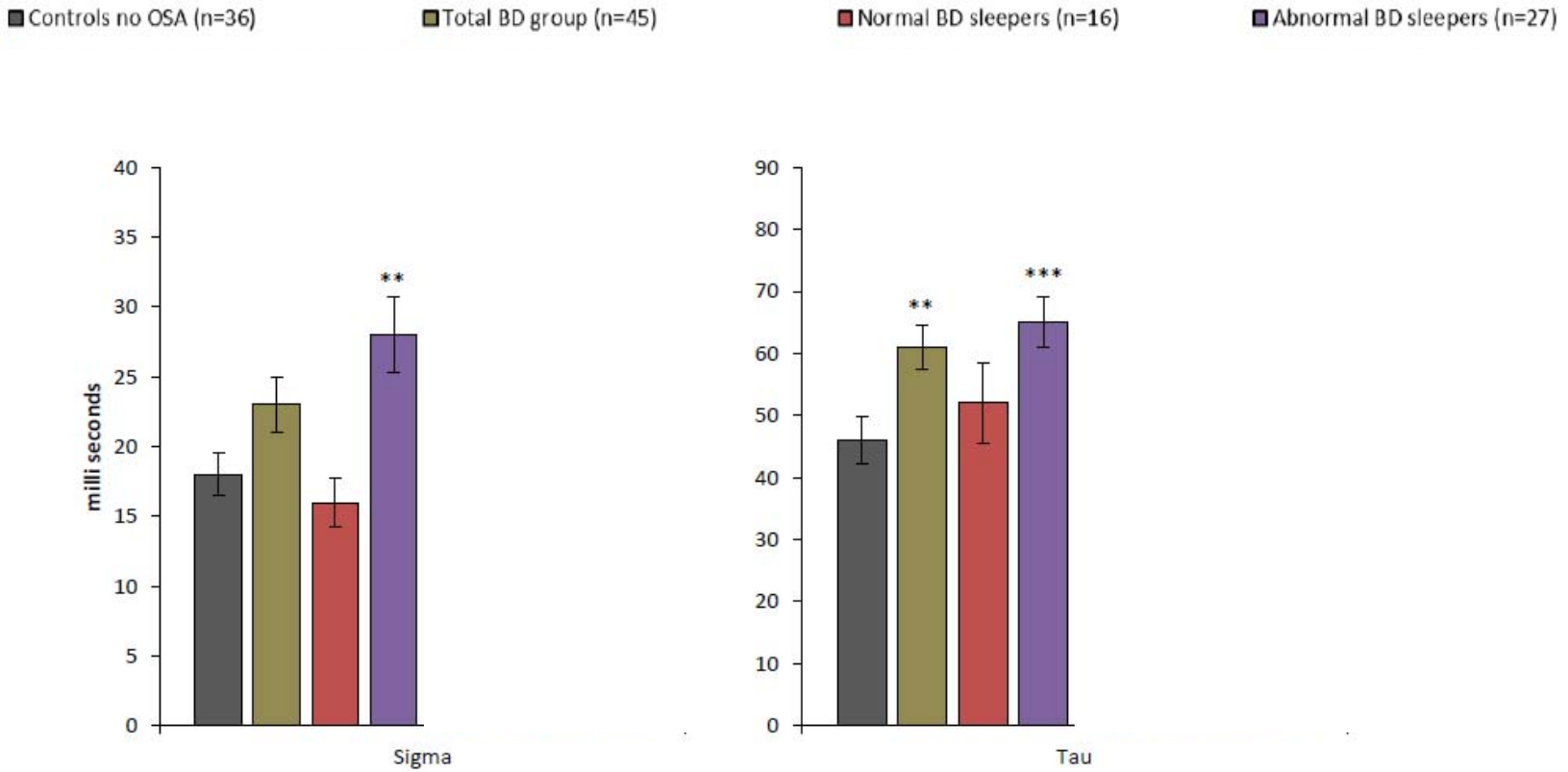


Figure 3.21 Ex-Gaussian analysis of intra-individual variability in mean PVT RT in controls and normal and abnormal BD sleepers

Effects of sleep disturbance on cognition in BD

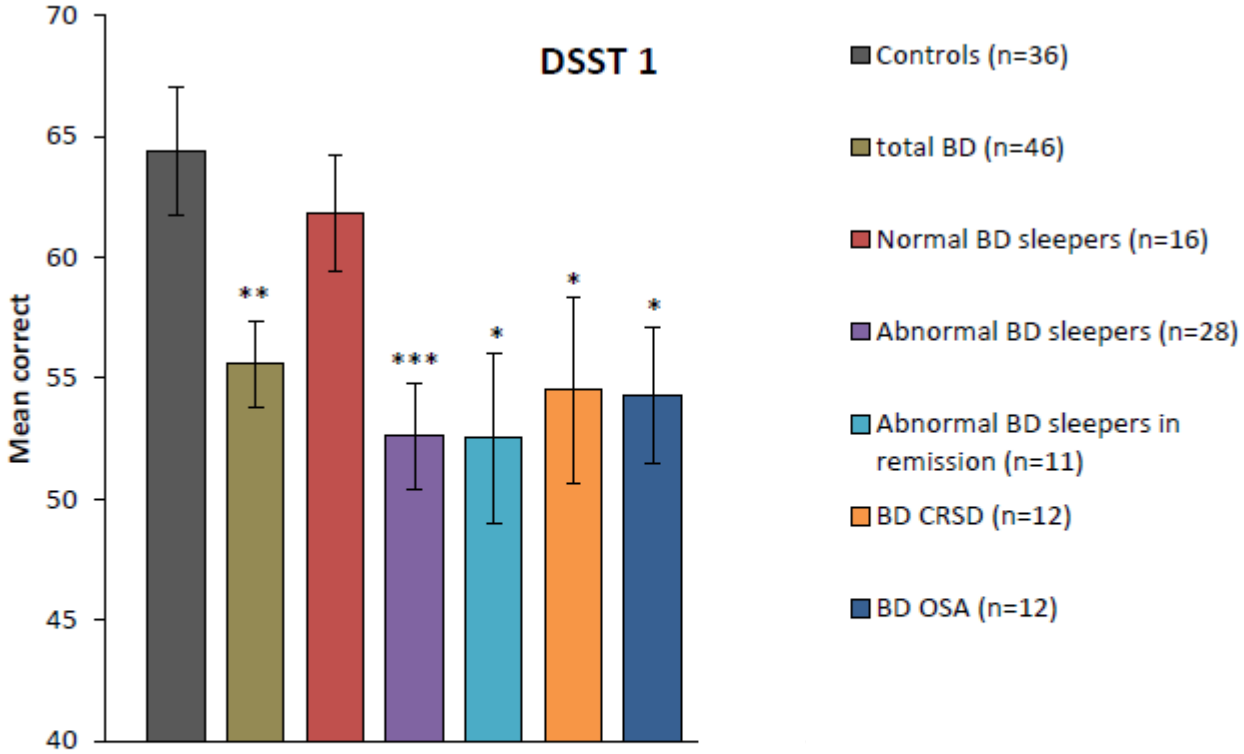
Attentional intra-individual variability



*p<0.05 vs. controls, **p<0.01 vs. controls ***p<0.001 vs. controls.

Effects of sleep disturbance on cognition in BD

Psychomotor speed



* p<0.05 vs controls, ** p<0.01 vs. controls, *** p<0.001 vs. controls

Summary

- Cognitive dysfunction is evident at the group level across multiple domains, but significant *inter-individual* variation in magnitude and profile
- Processes are hierarchically organised - core deficits underpinning the broader profile?
- Important to consider intra-individual variability – especially RT
- Only evident in patients with sleep disturbance – potential therapeutic intervention?


Steinan *et al. Trials* 2014, **15**:24
http://www.trialsjournal.com/content/15/1/24

TRIALS

STUDY PROTOCOL Open Access

Cognitive behavioral therapy for insomnia in euthymic bipolar disorder: study protocol for a randomized controlled trial

Mette Kvisten Steinan[1,2*], Karoline Krane-Gartiser[1], Knut Langsrud[1,2], Trond Sand[1,2], Håvard Kallestad[1,2] and Gunnar Morken[1,2]

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Christchurch, NZ

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