Robust cognitive neuroscience constructs and comorbidity: can they help?

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“Child psych is weird…”

“I just don’t get it…”

“Just what are they on about…”
"Hello, Emily. This is Gladys Murphy up the street. Fine, thanks . . . Say, could you go to your window and describe what's in my front yard?"
Types of ADHD

- combined type

- predominantly inattentive type

- predominantly hyperactive-impulsive type
Comorbidity of ADHD

- language-based learning disorders
- oppositional-defiant or conduct disorders
- anxiety and depressive symptoms through to disorders
- clumsiness through to developmental coordination disorder
‘Man is a riddle
not because he is an animal,
not because he is a social being,
not as part of nature and society.

It is as a person that he is a riddle – just that precisely;
it is because he possesses personality’

Nikolai Berdyaev (1944)
Nomothetic aspects of phenomena:

-those features of a given, particular phenomenon that are able to be validly and reliably demonstrated in groups of individuals with a particular disorder or a range of disorders

-**amenable** to the science of systematic observation and experiment

Ideographic aspects of the individual:

-those features of a given, particular individual that are not able to be validly and reliably demonstrated in groups of individuals with a particular disorder or a range of disorders

*that is*

aspects of an individual can be **truly unique**

-**not easily amenable** to the science of systematic observation and experiment
Case studies: anecdotal, unrepeatable, uncontrolled, unrepresentative, subjectively interpreted

Individual history examination may identify pattern(s) that are predictive of future behaviour, feelings and attitudes (ideographic approach), while examination of group differences (nomothetic approach) may not be applicable to the individual because psychological causation is always personal and never actuarial-generalisations are not binding on the individual
Allport GW. 1947. The use of personal documents in psychological science.
New York: Social Science Research Council
Three broad theoretical influences in the field of child and adolescent psychiatry

**Ideographic models**
- Psychodynamic theory and practice
- Family and social systems theory and practice

**Nomothetic model**
- Developmental psychopathology
Psychodynamic theory and practice

- **valid focus** on the human being as subject and inter-subjective states

-primarily concerned with the *interaction between* the conscious and unconscious aspects of the human mind

- systematic, formulated and scientific knowledge base

-free association and interpretation are key assessment and treatment tools, respectively

-monitoring of treatment resides primarily with the individual in the treatment process rather than with the clinician

-no clear biological risk factors or resilience factors identified

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Family and social systems theory and practice

- **valid focus** on human interpersonal systems

- primarily concerned with the *interdependence of relationships* in an interpersonal system governed by processes of circular causality and homeostasis

- systematic, formulated and scientific knowledge base

- aims of treatment are symptom removal from an identified individual; decreased family distress; improved communication; increased flexibility; increased problem solving

- monitoring of treatment resides primarily with the individual in the treatment process rather than with the clinician

- no clear biological risk factors or resilience factors identified (Hayes, 1991)

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Developmental psychopathology
- ‘an evolving interdisciplinary scientific perspective that elucidates the interplay between the biological, psychological and social contexts of normal and abnormal development across the life course’ (Cicchetti, 2001)
  - equifinality: more than one precursor/antecedent being associated with a given factor
    ADHD-CT
    ANX EF LBLD
  - multifinality: a given precursor/antecedent being associated with multiple factors
    ANX ADHD-CT ODD/CD
    LBLD
Developmental psychopathology

-risk factors and resilience factors are *interdependent* in a given individual (e.g., a hostile critical primary caregiver relationship may be a risk factor at age 3 and a resilience factor at age 13 in a given individual)

-assessment and treatment involves [1] identifying biological, psychological, social, cultural and developmental risk and resilience factors and their *relative importance* in a given individual and [2] *biological and psychological* treatments used alone or in conjunction to achieve specific goals informed by the relative priorities of these risk and resilience factors

-monitoring of treatment resides primarily with the *clinician* in association with the individual in the treatment process

-clear biological risk factors or resilience factors identified
Currently,

the first two ideographic theoretical influences are in the ascendancy in the field although the nomothetic developmental psychopathology model is gaining credibility

its credibility is primarily due to its consonance with the international movement towards understandable and complimentary modes of service delivery in paediatric, youth and adult psychiatric services
Clinical phenotyping

current need to be more *specific* with key phenomena defined:

- putative primary core symptoms/signs of a given disorder associated with its putative core *pathophysiology*

  versus

  secondary comorbid symptoms/signs associated with *maladaptive* pathophysiological responses to the primary disorder

  versus

  primary and secondary symptoms/signs sharing a *common* aetiological vulnerability

  versus

  *no association*
Robust Cognitive Neuroscience constructs

- sensible, straight forward, not given to or confused by subtleties; strong

- *ongoing process of refining* measures of verbal and visuospatial working memory, motor response inhibition as the most robust of executive function constructs

- increased recognition of *non-human primate derived models* of executive function, given well defined brain behaviour relationships through single neuronal firing rate studies and high prevalence of language-based learning difficulties in psychiatric clinical populations

- more *targeted* use of specific measures of executive function (eg visuospatial working memory in children with ADHD-CT given 30%+ rates of language based learning difficulties)
The conceptual problem of comorbidity

Comorbid disorders are separate disorders

Comorbid disorders are secondary disorders

ADHD → anxiety disorders / depressive disorders

ADHD ← anxiety disorders / depressive disorders

Comorbid disorders share common antecedent

ADHD → anxiety disorders / depressive disorders

Working memory deficits

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The conceptual problem of comorbidity

- comorbid disorders are separate disorders

- overwhelming evidence of a greater than chance association of ADHD and anxiety disorders / depressive disorders
The conceptual problem of comorbidity

- comorbid disorders are secondary disorders

ADHD ➔ anxiety disorders / depressive disorders
FIGURE 8.1 The prefrontal, parietal, and temporal association cortices form interconnected networks that play complementary roles in attentional processing.
Figure 16.1. Central organisation of the frontal–subcortical circuits.

Figure 16.2. Organisation of the frontal–subcortical circuits (see also Cummings, 1993). (NB: indirect circuits of the substantia nigra and subthalamic nucleus are not shown.)
The conceptual problem of comorbidity

- comorbid disorders are secondary disorders

  ADHD ← anxiety disorders / depressive disorders
Prefrontal cortex function

Behavoural symptom level

Prefrontal cortex dysfunction
Anxiety – low/high
Depression - low

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The conceptual problem of comorbidity

- comorbid disorders share common antecedent

**ADHD**  anxiety disorders / depressive disorders

working memory deficits
Working Memory

defined aspects

- amenable to componential analysis

- able to make inferences about underlying brain function
Spatial Working Memory and PFC function

[1] relationship constrained by

studies of single neuronal firing rates in alert primates

studies of behaviour following focal PFC lesions in adult humans

studies of patterns of regional cerebral blood flow in healthy humans performing spatial working memory tests

[2] largely non-verbal construct
Anxiety

ADHD-CT and anxiety

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R² = 0.8674

R² = 0.9867

Age (months)

BSE - total

Anxiety

ADHD-CT and anxiety

ADHD-CT
Graph showing the relationship between BSE task difficulty and BSE total score for different conditions:

- **Dysthymic disorder**
- **ADHD-CT and dysthymic disorder**
- **ADHD-CT**

The x-axis represents BSE task difficulty, and the y-axis represents BSE total score. The graph includes error bars for each data point.
$R^2 = 0.8055$

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The conceptual problem of comorbidity

- comorbid disorders share common antecedent

ADHD                   anxiety disorders / depressive disorders

working memory deficits
Greater activation for Control than ADHD group.

<table>
<thead>
<tr>
<th>Region</th>
<th>BA</th>
<th>x</th>
<th>y</th>
<th>z</th>
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<tbody>
<tr>
<td>Left Prefrontal</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Caudate Head</td>
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<td>54</td>
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<td>-30</td>
<td>30</td>
<td>12</td>
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<tr>
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<td>47</td>
<td>18</td>
<td>12</td>
<td>-21</td>
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<tr>
<td>Right Parietal</td>
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<td>Inf Parietal Lob.</td>
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<td>42</td>
<td>-57</td>
<td>39</td>
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<td>Sup Parietal Lob.</td>
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<td>Occipital</td>
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<tr>
<td>Left Precuneus</td>
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<td>-12</td>
<td>-81</td>
<td>42</td>
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<tr>
<td>Right Cuneus</td>
<td>19</td>
<td>15</td>
<td>-84</td>
<td>33</td>
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Greater activation for ADHD than Control group.

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<th>x</th>
<th>y</th>
<th>z</th>
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<tr>
<td>Left Temporal</td>
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<tr>
<td>L Sup Temporal Gyr.</td>
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<td>-27</td>
<td>6</td>
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<tr>
<td>L Mid Temporal Gyr.</td>
<td>39</td>
<td>-48</td>
<td>-60</td>
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</table>
Percentage correct (mean)

- Controls
- ADHD M
- ADHD U

MTS  DMTS 0  DMTS 4  DMTS 12
Control vs ADHD-U
Control vs ADHD-M
ADHD-U vs ADHD-M
Control vs ADHD-U
Control vs ADHD-M
ADHD-U vs ADHD-M

Effect sizes (Cohen's d)

Before
After

0.94
0.74
0.04
0.81
0.79
0.34
0.26

-0.2
0.45
0.47
0.4
0.26

-0.4
-0.2
0
0.2
0.4
0.6
0.8
1
Delayed Matching To Sample (DMTS) (mean correct responses) at simultaneous and three delay conditions across the three groups, covarying for age
DMTS (mean correct responses) of the three delay conditions across the three groups, covarying for the simultaneous matching to sample:

Level of delay (0, 4, 12 seconds delay)
[a] Wilks’ $\lambda = .80$, $F(4, 104) = 3.17$, $p = .02$
[b] 12: MDD > DD, control
Cohen’s d = .73
Cognitive neuroscience

-key future step:
  parsing of key constructs such as working memory

(ab)/normal developmental trajectories mapped
which will aid the determination of

*whether deviant or delayed development,
*developmental stage specific or generalised,
*primary disorder phenotype specific abnormalities versus secondary comorbid disorders
Summary

-progressively better definition of
  * clinical phenotyping, particularly of primary versus secondary phenomena (aided by theoretical models)
  * cognitive neuroscience constructs
  * functional neuroimaging
  * molecular genetic candidate gene polymorphisms

-will aid the definition of (ab)/normal developmental trajectories, whether development is deviant or delayed, and whether alterations are developmental stage specific or generalised

-and will aid the determination of threshold effects and primary risk factors (core pathophysiology) versus secondary (absent) resilience factors ((mal)/adaptive physiological processes)
Summary

-in turn, the process of illuminating developmental neuroanatomical physiological processes and their dysfunction will be *facilitated*

Thus, the evidence-based (nomothetic) approach is developing and needs to be in *balance* with the individual-based (ideographic) approach so the subjective, objective, inter-subjective and interpersonal domains form the basis of assessment, treatment and monitoring of treatment

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Nomothetic  

Ideographic  

Comprehensive assessment, treatment and monitoring of treatment

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