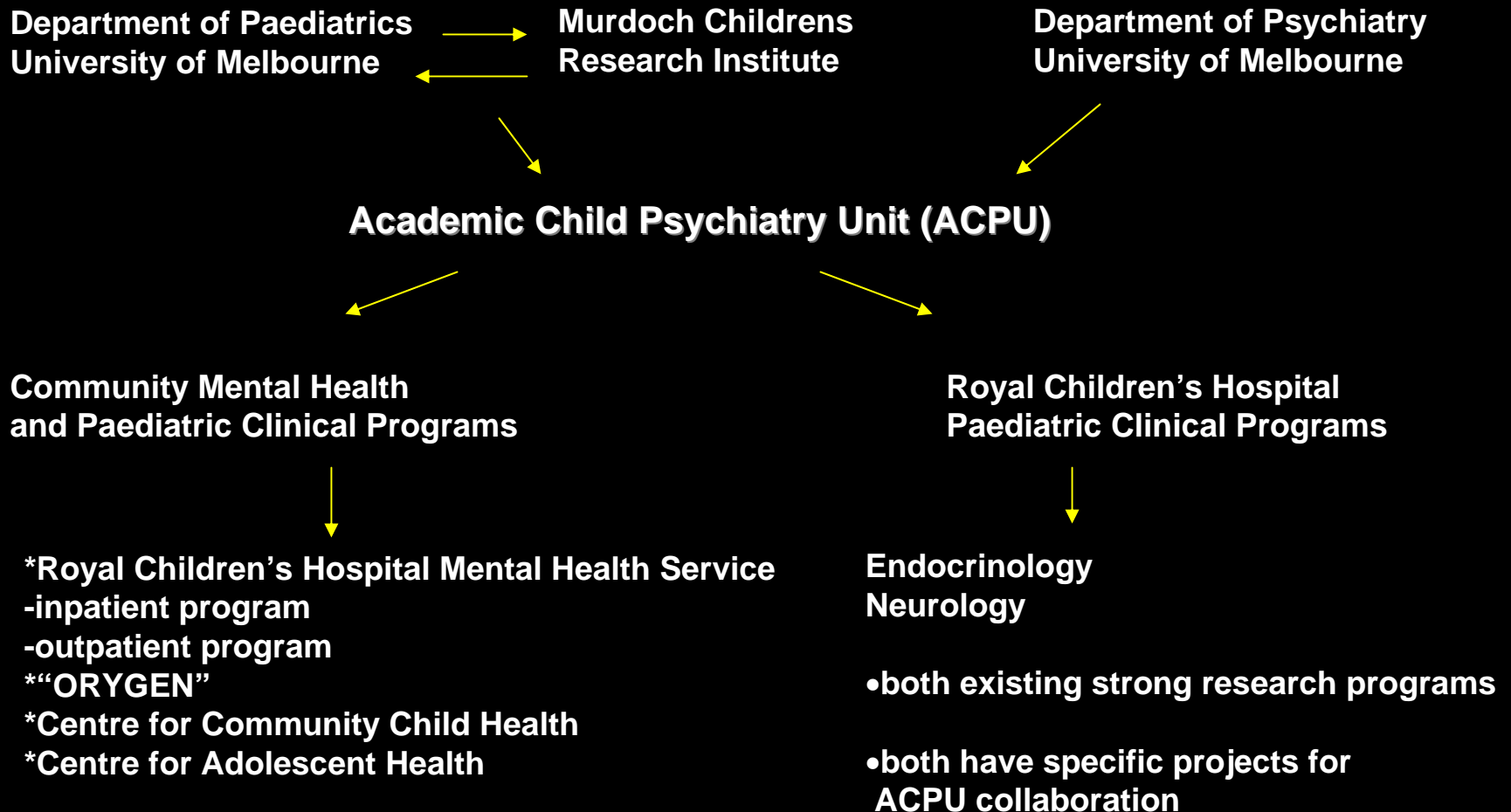


Academic Child Psychiatry Unit (ACPU)

- 1. Organisational and schematic overview of the ACPU**
- 2. Foundational theoretical model of research within the ACPU**
- 3. Disorder-focused research clinics within the ACPU**
- 4. Current examples of our research**

1. Organisational and schematic overview of the ACPU



2. Foundational theoretical model of research within the ACPU

[1] Risk and [2] resilience factors need to be determined at the levels of

- a. Clinical phenomena (symptoms and signs),**
- b. Biological measures and**
- c. Environmental measures**

The above risk and resilience factors need to be studied within and across specific developmental stages to determine whether they are stage-specific or stage-independent. That is a risk factor at one developmental stage may be a resilience factor at another.

Level of enquiry

Clinical phenomena:

symptoms and signs

Risk factors

Resilience factors

Biological phenomena:

IQ

Verbal IQ

Performance IQ

Language-based

spelling

Learning Skills

arithmetic

reading

Cognitive neuroscience constructs

spatial memory

spatial working memory

Neurophysiological constructs

pro-saccades

anti-saccades

Brain neuronal Networks

fMRI parieto-frontal

fMRI temporo-frontal paradigms

Molecular genetics

candidate genes

(eg, COMT val/met polymorphism and working memory performance)

Developmental stage:

Specific versus

Non-specific

Level of enquiry

Environmental phenomena:

Risk factors

Resilience factors

Parental symptoms signs

Psychopathology

Parental relationships

Problem solving

Family relationships

Adaptability

Peer relationships

Confiding nature

Developmental stage:

Specific versus

Non-specific

3. Disorder-focused research clinics within the ACPU

Child psychiatric disorders are based on [1] the presence of symptom patterns, based on multi-informant reports (eg, parent, child, teacher) and [2] the presence of impairment in a given child's academic, interpersonal, family and social development directly relate to the presence of the above symptom patterns.

The four community-based ACPU clinics are structured around key high prevalence and high risk child psychiatric disorders that are frequently treatment non-responsive.

■ **Disruptive Behaviour Disorders Clinic**

- **Attention Deficit Hyperactivity Disorder (combined type) (ADHD-CT)**
- **Oppositional defiant disorder**
- **Conduct disorder**

■ **Depressive Disorders Clinic**

- **Dysthymic disorder (primarily pre-pubertal)**
- **Major depressive disorder (primarily post-pubertal)**

■ **Anxiety Disorders Clinic**

- **Generalised Anxiety Disorder**
- **Separation Anxiety Disorder**
- **Specific phobia**
- **Social phobia**

- **Obsessive Compulsive Disorder**

- **Post Traumatic Stress Disorder**

- **Panic Disorder**

■ **Autistic Disorders Clinic**

- **High Functioning Autistic Disorder**
- **Asperger's Disorder**

The one hospital-based ACPU clinic will be structured around

(a) single gene disorders

(eg, Turner Syndrome, Prader-Willi syndrome)

(b) a specific physiological/pathophysiological process

(eg, adrenarche, gametogenesis)

(c) A specific syndrome

(eg, new daily persistent headache) or specific disorder

Current biological contributions : Summary

progressively better definition of

- * clinical phenotyping, particularly of primary versus secondary phenomena (aided by theoretical models)
- * cognitive neuroscience and neurophysiological constructs
- * functional and structural 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)

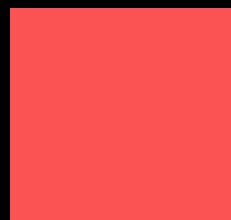
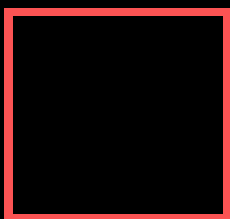
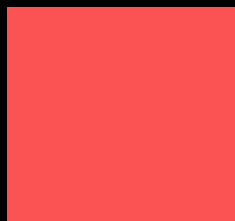
Current biological contributions : Summary

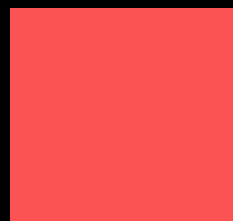
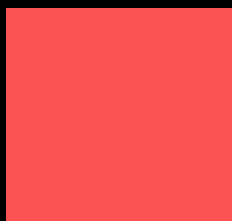
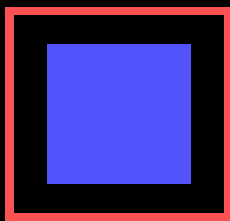
in turn, the process of illuminating developmental neuroanatomical physiological processes and their dysfunction will be *facilitated*

Current biological contributions

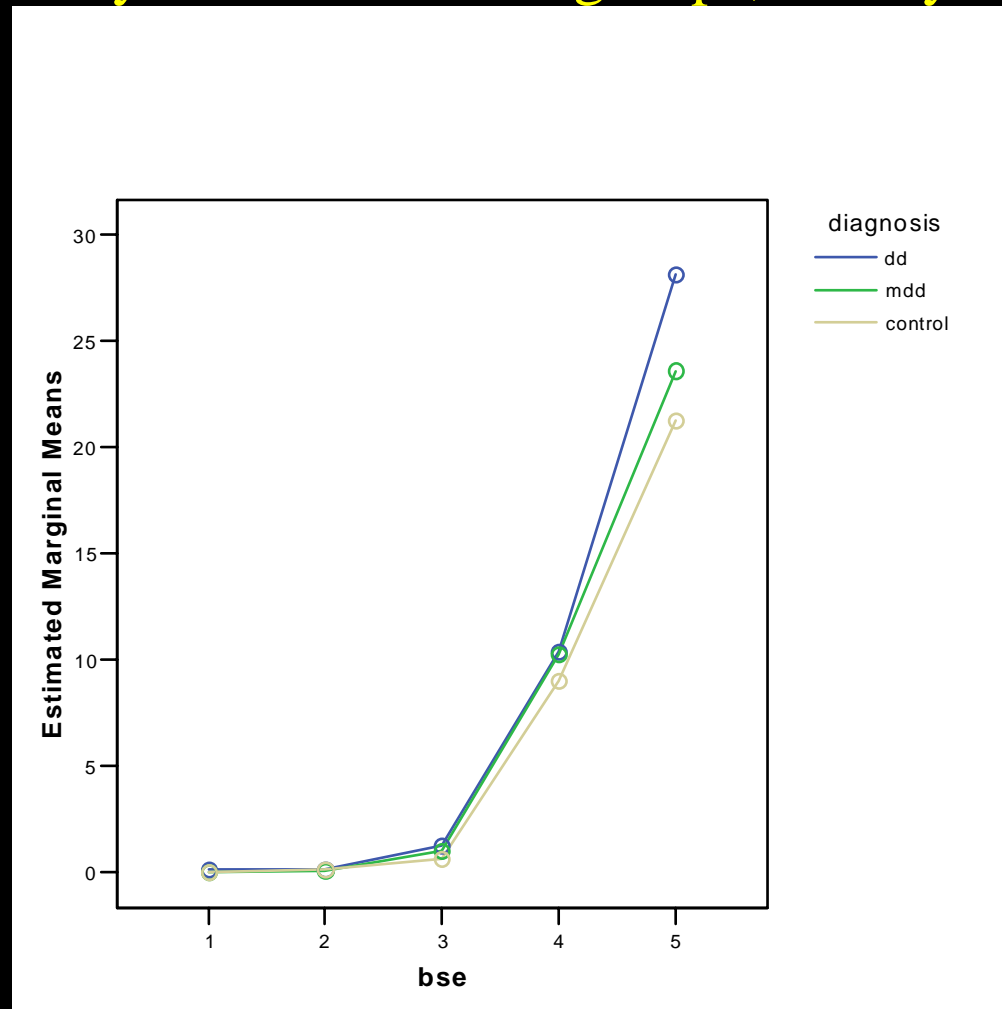
Cognitive Neuroscience

- 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)





Between Search Errors (BSE) (mean) at each level of difficulty across the three groups, covarying for age



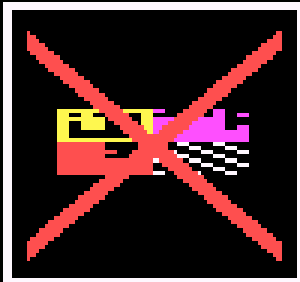
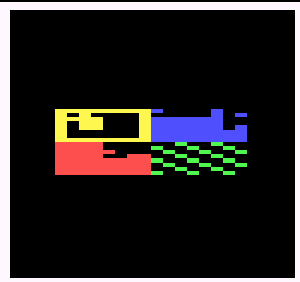
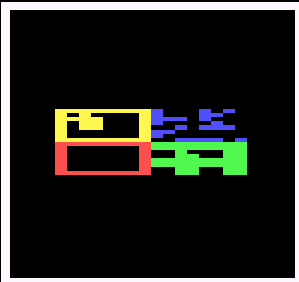
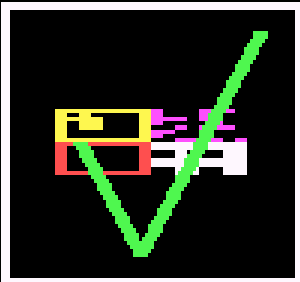
Level of difficulty (number of boxes)

[a] Wilks' $\lambda = .89$, $F(8, 272) = 1.77$, $p = .05$, partial $\eta^2 = .06$

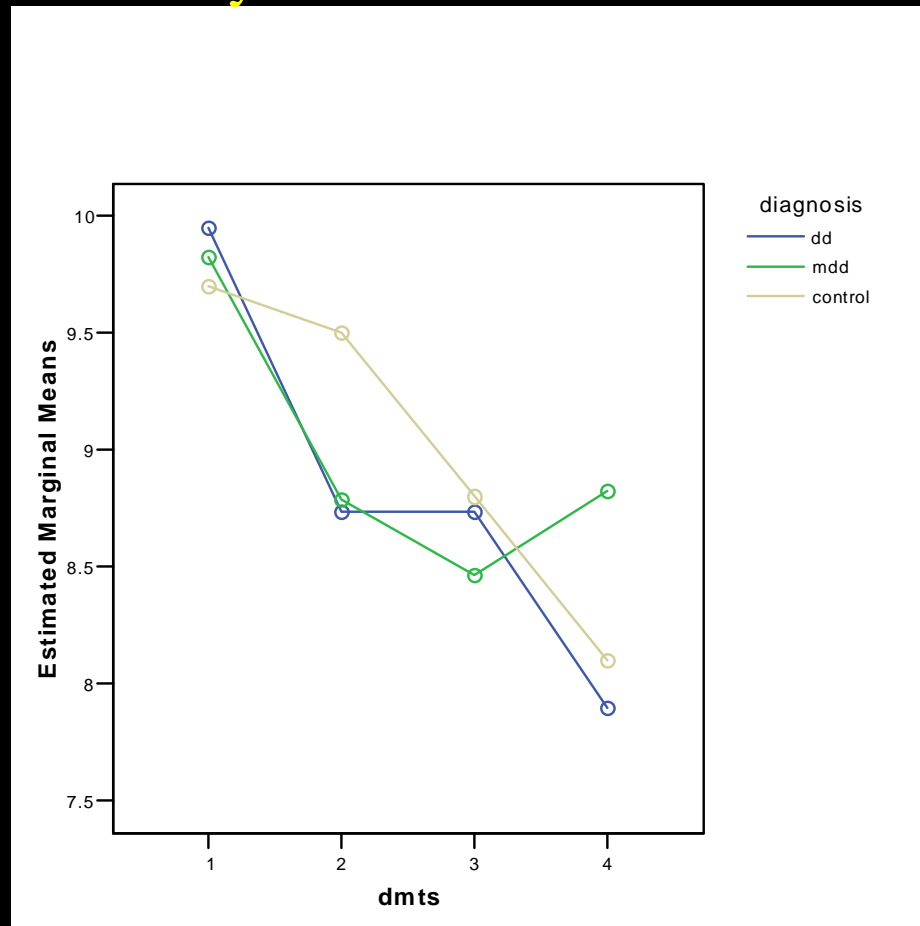
[b] Dysthymic disorder > controls $F(2, 176) = 3.32$, $p = .04$,

Cohen's $d = .81$

CORRECT



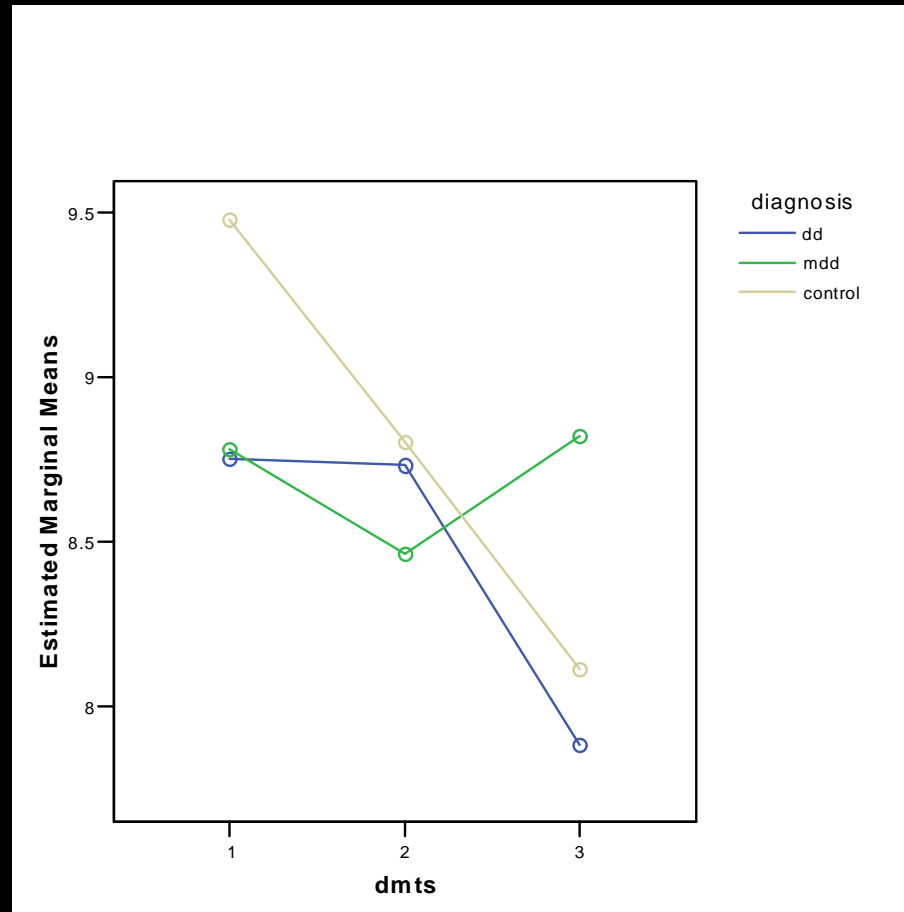
Delayed Matching To Sample(DMTS) (mean correct responses) at simultaneous and three delay conditions across the three groups: Age \geq 13 years



Level of delay (simultaneous, 0,4,12 seconds)
[a] Wilks' $\lambda = .76$, $F(6, 104)=2.62$, $p=.02$,
0: controls $>$ DD, MDD; 12: MDD $>$ DD
cohen's $d = .66/.65; .73$

Delayed Matching To Sample (DMTS) (mean correct responses) of the three delay conditions across the three groups, covarying for the simultaneous matching to sample:

Age \geq 13 years



Level of delay (0,4,12 seconds delay)

[a] Wilks' $\lambda = .80$, $F(4, 104)=3.17$, $p=.02$,

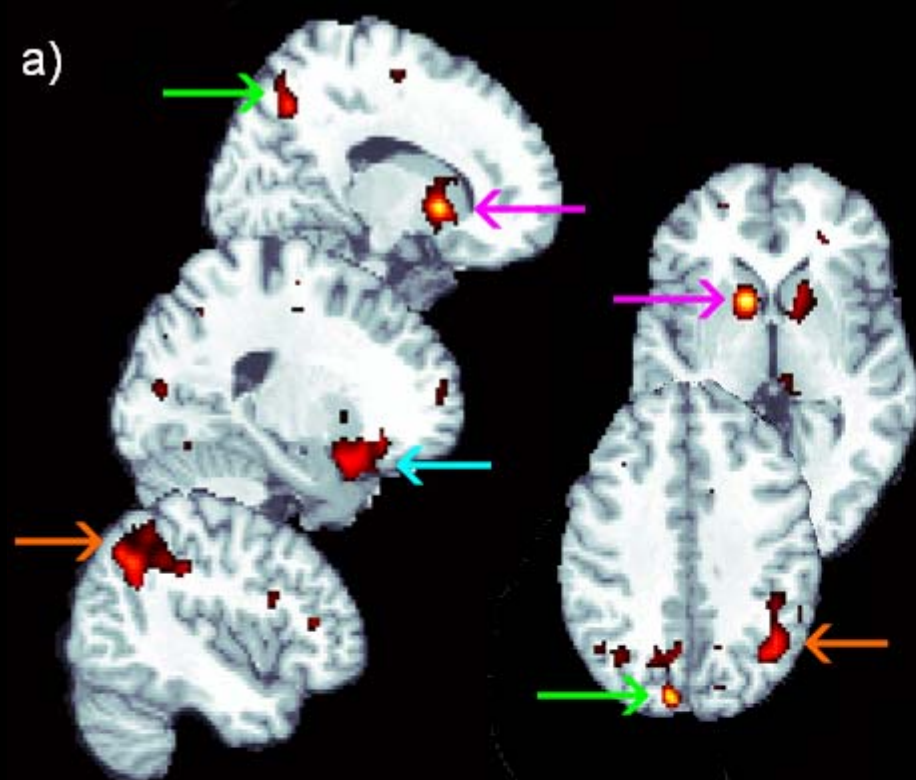
[b] 0: controls $>$ DD, MDD; 12: MDD $>$ DD

cohen's $d = .66/.65; .73$

Current biological contributions

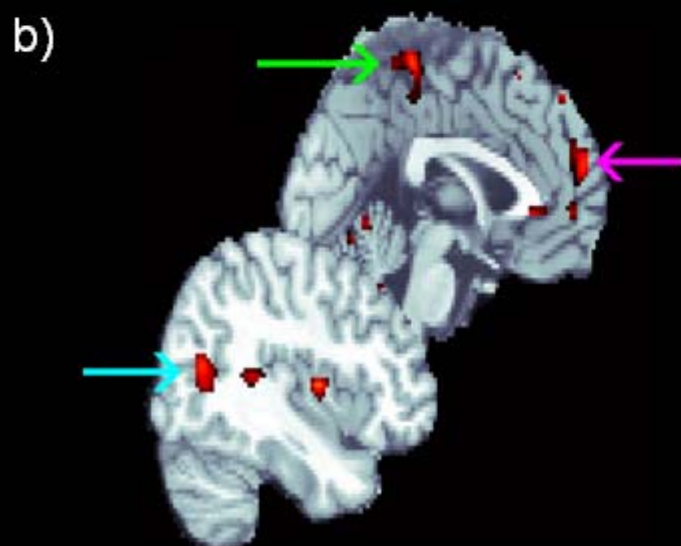
Neuroimaging

- aided the *localisation* and investigation of these neurodevelopmental anatomical processes
- structural imaging (primarily MRI) has consistently implicated particular brain regions (caudate nucleus, DLPFC, AC, H, cerebellum) in a range of disorders, the most robust studies suggesting that there are *ongoing* neuropathological changes in disorders such as schizophrenia while there are *discrete* changes in others such as ADHD
- functional imaging (fMRI and MRS) is increasingly useful to investigate in vivo activation of *neural networks* associated with defined cognitive neuroscience tasks (fMRI) and in vivo *markers of neurochemistry* (MRS)



Greater activation for Control than ADHD group.

Region	BA	x	y	z
● Left Prefrontal				
Caudate Head		-15	12	0
Sup Frontal Gyr.	10	-27	54	3
Inf Frontal Gyr.	46	-30	30	12
● Right Prefrontal				
Ventral Inf Frontal Gyr.	47	18	12	-21
● Right Parietal				
Inf Parietal Lob.	40	42	-57	39
Sup Parietal Lob.	7	36	-60	51
● Occipital				
Left Precuneus	19	-12	-81	42
Right Cuneus	19	15	-84	33



Greater activation for ADHD than Control group.

Region	BA	x	y	z
● Medial Sup Frontal Gyr.	10	-9	63	15
● Posterior Cingulate Gyr.	31	18	-24	30
● Left Temporal				
L Sup Temporal Gyr.	13	-36	-27	6
L Mid Temporal Gyr.	39	-48	-60	9

Current biological contributions

Molecular Genetics

-primarily association studies have shown a moderate strength association between

key *catecholamine transporter polymorphisms* and high and low prevalence *psychiatric disorders*

**dopamine : ADHD*

**noradrenaline : anxiety disorders*

**serotonin : anxiety disorders, depressive disorders*

COMTval/met : anxiety disorders, schizophrenia

-*imprecise phenotyping* is the primary limitation

Current biological contributions

Molecular Genetics

-a few gene-environment interactions have been reported

***MAOA : maltreatment : CD/ASPD**

***5HTT : lifelong stress events : depressive disorders and suicide**

***COMT : cannabis : psychotic symptoms, schizophreniform disorder**

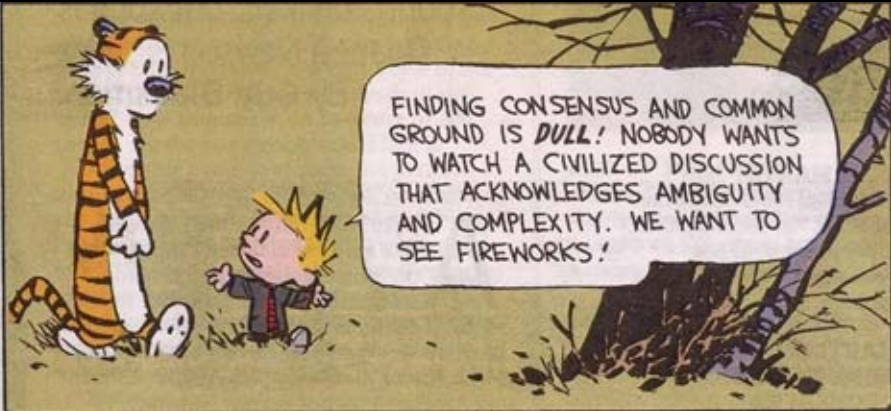
-again *specificity* of the definition of the environmental event and the resultant phenotypic expression are the primary limitations

-association studies of cognitive neuroscience constructs and fMRI neural network activation patterns have begun:

***verbal working memory : COMT**

***verbal working memory fMRI : DLPFC activation**

again *specificity* of the definition of the cognitive neuroscience construct is the primary limitation



calvin and hobbes

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