Delusions, cognitive mechanisms, and the prodromal phase of psychosis.

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Content of talk

- Psychosis, delusions, and schizophrenia: some clinical psychiatry
- The science of psychosis: neurodevelopment and dopamine
- Cognitive models of delusions and relationship to neuroscience
- Data of cognitive biases related to delusion formation in prodromal sample.

Psychosis

- Mental disorder in which the thoughts, affective response or ability to recognize reality, and ability to communicate and relate to others are sufficiently impaired to interfere grossly with the capacity to deal with reality; the classical characteristics of psychosis are impaired reality testing, hallucinations, delusions, and illusions.

DSM IV on psychosis

- ‘disorders in this section are all characterized by having psychotic symptoms as defining feature’.
- ‘the term *psychotic* has historically received a number of different definitions,[…]. The narrowest definition of *psychotic* is restricted to delusions or prominent hallucinations, with the hallucinations occurring in the absence of insight into their pathological nature’.

DSM IV on psychosis

- ‘A slightly less restrictive definition would also include prominent hallucinations that the individual realizes are hallucinatory experiences. Broader still is a definition that includes other positive symptoms of schizophrenia (i.e., disorganized speech, grossly disorganized or catatonic behaviour.)’

Delusions

- ‘A delusion is a false, unshakeable idea or belief which is out of keeping with the patient’s educational, cultural and social background; it is held with extraordinary conviction and subjective certainty’ (Sims, 1995).
- ‘A delusion is a belief that is firmly held on inadequate grounds, is not affected by rational argument or evidence to the contrary, and is not a conventional belief that the person might be expected to hold given her educational, cultural, and religious background’ (OTP, 2006).

Classifying delusions

- Primary (‘delusions’) vs secondary (delusion-like)
- Schneiderian
- Theme
- Degree of conviction/fixity – partial, complete.

Jaspers on delusions 1913

- *Verstehen*
- Dilthey's hermeneutics 'interpretative understanding' 'empathy'.
- Primary – un-understandable, psychologically irreducible.
- Secondary/delusion-like – understandable, arise from other psychic phenomena

Schneiderian symptoms

- FRS
- If occur in absence of coarse brain disease, then will call it Schizophrenia.
- 2nd rank symptoms also allow diagnosis of Schizophrenia if ‘certain combinations or numbers’.
- Emphasises that although recovery can occur, exceptional.

Schneider's First Rank Symptoms

- Thought echo
- 3rd person auditory hallucinations/commentary
- Somatic hallucinations
- Thought withdrawal or insertion
- Thought broadcasting
- Delusional perception
- Made feelings/acts

Typical contents and themes

- Persecution
- Reference
- Grandiose
- Guilt
- Hypocondriacal
- Nihilistic (Cotard's)
- Religious
- Delusional misidentification (Capgras, Fregoli).
- Jealous (Othello)
- Sexual/amorous (erotomania – de Clerembeault's)
- Dysmorphophobia
- Delusions of control (passivity)
- Thought withdrawal, thought insertion, thought broadcasting

Clinical features of Schizophrenia

- Defined largely by duration of illness (6/12 or 1/12 depending on DSM/ICD)
- Course of illness over time
- Presence of certain psychotic symptoms (weighted towards FRS)
- Absence of prominent mood disorder
- Absence of medical/organic illness causing psychosis.

DSM IV Sz

- 1 of bizarre delusions or Schneiderian hallucinations or
- 2 of delusions, hallucinations, disorganized speech/behaviour, negative features.
- + social/occupational dysfunction
- 6/12 duration
- Exclude: mood disorder, substance abuse, PDD.

ICD-10 Sz

- 1 Schneiderian delusion/hallucinations or
- 2 of hallucinations, disorganized speech, negative features, catatonic features.
- 1/12 duration
- Exclude: mood disorder, substance abuse, PDD, organic brain disease.

Neurodevelopmental Model

- Weinberger in US and Murray in UK
- ‘genes involved in neurodevelopment and/or environmental insults in early life lead to aberrant brain development, which in turn predisposes to the later onset of psychosis’
- ‘doomed from the womb’
- Therapeutic pessimism, palliative psychiatry

Neurodevelopmental model

- Dominant paradigm guiding research since 1980's.
- Sz result of abnormal brain development, this in turn secondary to genetic predisposition and early environmental factors.
- Ventricular enlargement static, altered cytoarchitecture and absence of gliosis suggests prenatal.
- Children who go on to develop Sz have impaired motor, intellectual, behavioural development.

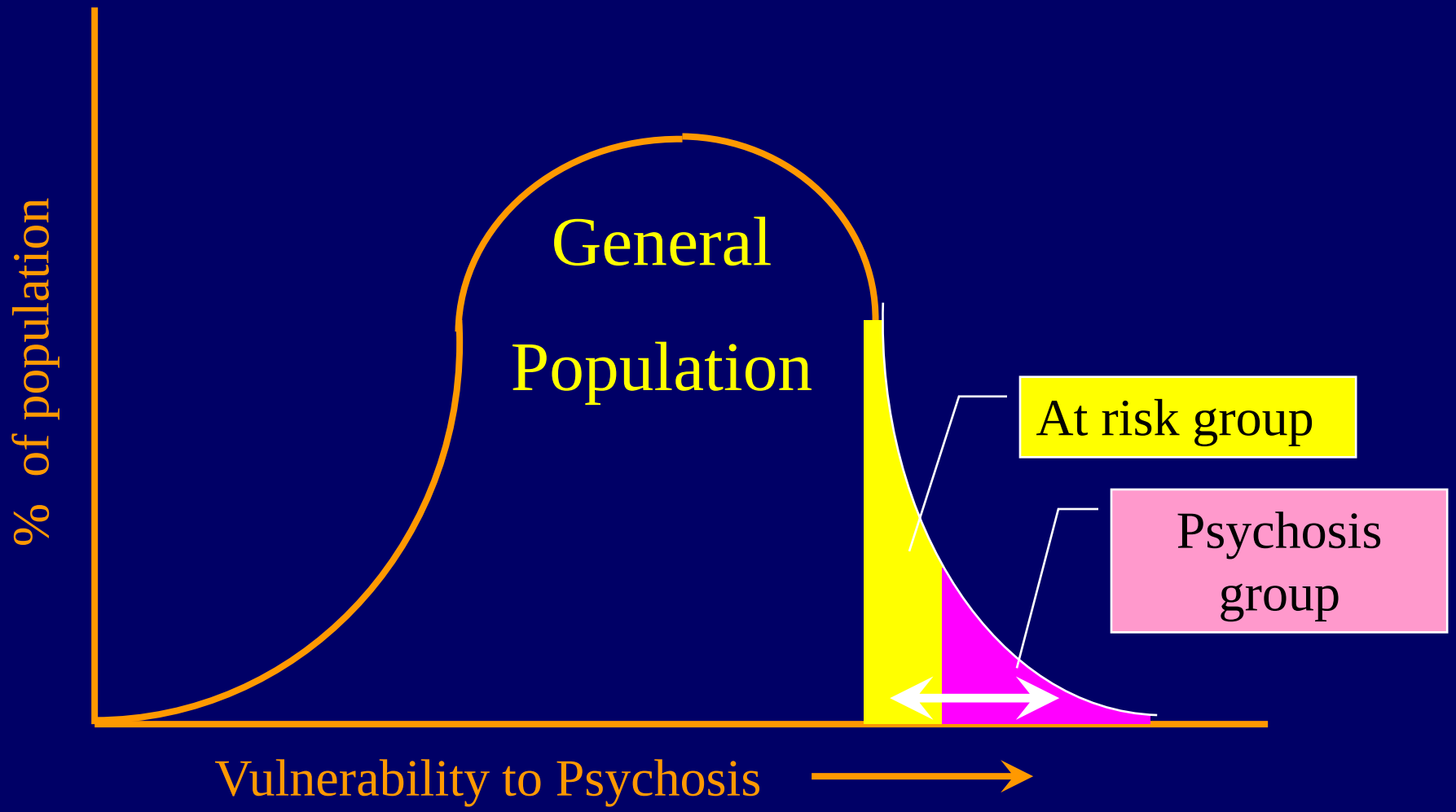
Signs pre-onset

- Developmental milestones
- Social interaction – solitary and anxious
- Cognitive impairments
- Quasi-psychotic symptoms in childhood

Challenges to the orthodoxy

- Social factors: urban upbringing, migration, bullying, racism, childhood sexual abuse, absent father.
- Continuum – factors associated with Sz also associated with psychotic experiences in normal population (single, urban, unemployed, cannabis, low IQ, poorer education, cannabis, alcohol, life events).
- ‘prodrome’ – helpseeking, symptoms, but not ‘case’.

General Population Risk for Psychosis



Problem of onset

- What converts developmentally impaired, socially isolated adolescent with odd ideas and experiences into a psychotic individual?
- Depression? Intensity? Neuropsychology?

- Cognitive schema and appraisal.

Dopamine as the ‘wind of the psychotic fire’: salience

- Hemsley, Gray, and Kapur
- ‘meaningful connections are created between temporary coincident external impressions or perceptions with thoughts that happen to be present, or events and recollections happening to occur at the same time’
- ? Early 90’s Gray, Hemsley posited that hippocampal damage would lead to dysregulation of mesolimbic dopamine system, and the false creation of ‘meaningful connections’ between coincident events.

Dopamine and normal mental life

- Mesolimbic dopamine provides significance or salience.
- Transforms an affectively neutral mental representation of a stimulus into an attractive or aversive one.
- External perceptual or internal mental
- ‘hedonic vector’ and ‘grabs the attention’
- An ‘is’ to a ‘towards which’ or ‘away from’

Psychosis and dopamine

- Dysregulated dopamine in psychosis
- Correlates with positive symptoms
- Correlate with response to medication (D2 antags).
- Psychosis increased, stimulus-independent release of dopamine leading to salience being granted to otherwise innocuous stimuli

Psychosis and dopamine

- In psychosis, cortico-limbic malfunction.
- Prefrontal cortex dysfunction and volume loss in amygdala and hippocampus.
- Excessive activity of limbic centres and loss of prefrontal ‘brake’?
- Increased dopamine, increased salience, paranoia and psychosis.

Risk for dopamine dysregulation

- Genes: neuregulin, dysbindin, DISC-1, COMT.
- Environmental insults: hippocampal size, sensitive dopamine system.
- Drugs: sensitization.
- Social: ‘social defeat’ – animal models inc. dopamine response, macaque monkeys – isolation, social subordination.

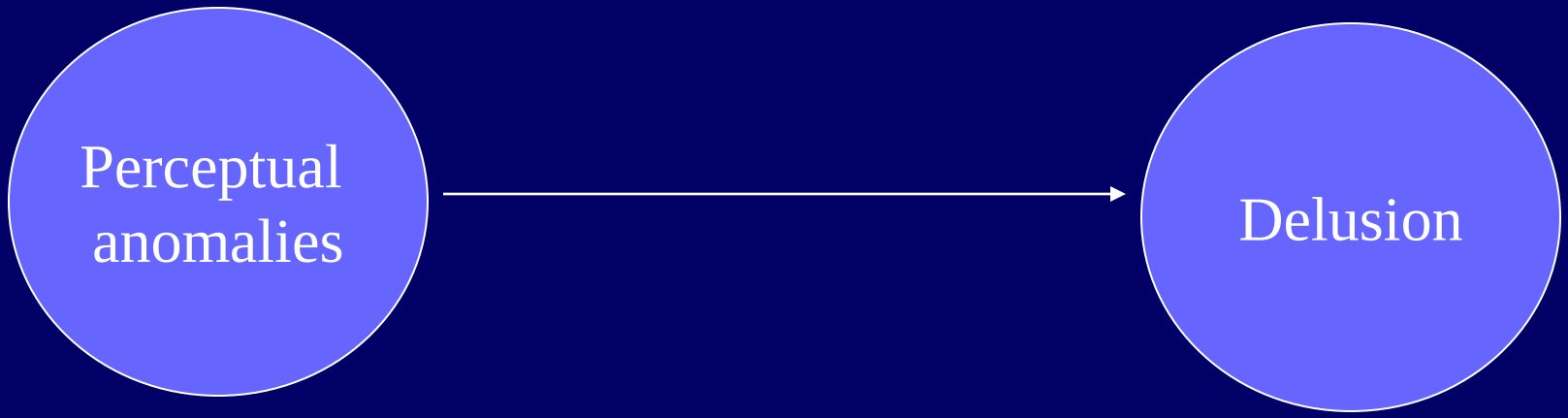
Maher and his theory of delusions

- ‘Basic cognitive dysfunction’ (Frith, Hemsley) first step: this leads to generation of ‘anomalous experiences’.
- Delusion is the result of an intact reasoning mechanism to make sense of anomalous experience. Delusion is an explanation.
- Two-stage model of delusions.

Cognitive models and dopamine

- Garety ‘basic cognitive dysfunction’ – Hemsley, Frith.
- Generates anomalous experiences
- ? Cognitive parallel of increased mesolimbic dopaminergic transmission and inappropriate salience ?
- “my thoughts get all jumbled up … Things are coming in too fast. I loose my grip and get lost. I am attending to everything at once and as a result do not attend to anything”.

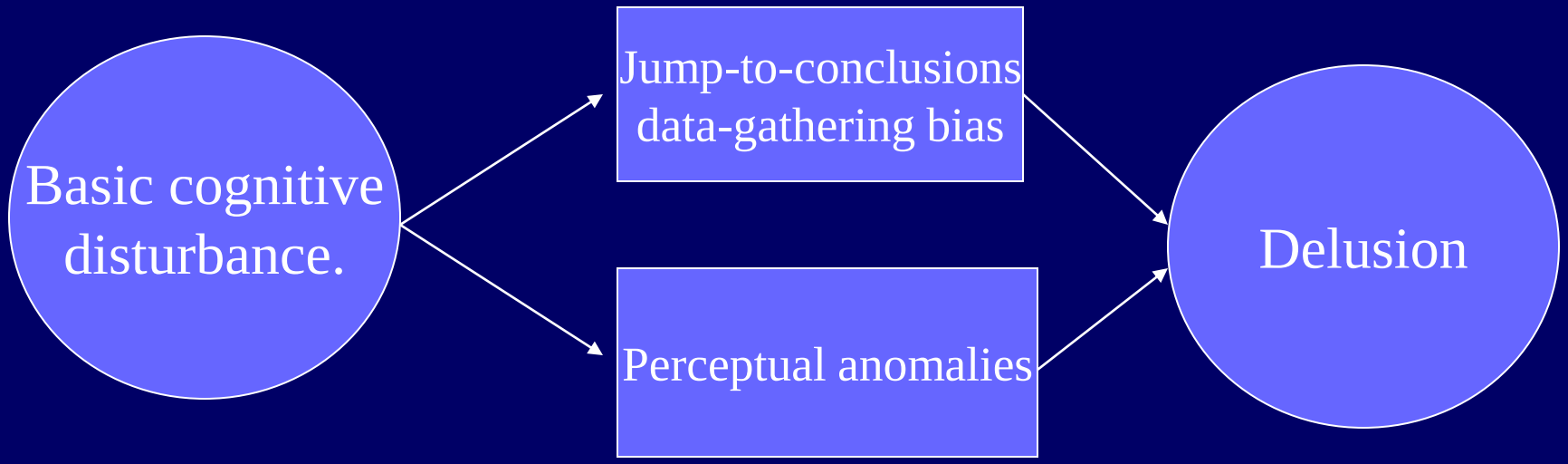
MAHER (92):



Post-Maher

- Maher's work huge impetus for research and therapy into the psychopathology of psychosis (Jaspers' 'ununderstandable'.)
- Current cognitive models (both theoretical and clinical) work within this model but refute the second stage (intact reasoning) and to some extent, the necessity of an anomalous experience.

GARETY & HEMSLEY (94):



Factors in stage 2

- Garety: jumping to conclusions and data gathering bias.
- Frith: ‘theory of mind’ and deficits in metarepresentation.
- Bentall: appraisal, misattribution and ‘defence’ against depression.
- Others: social isolation, metacognition, intolerance of ambiguity.

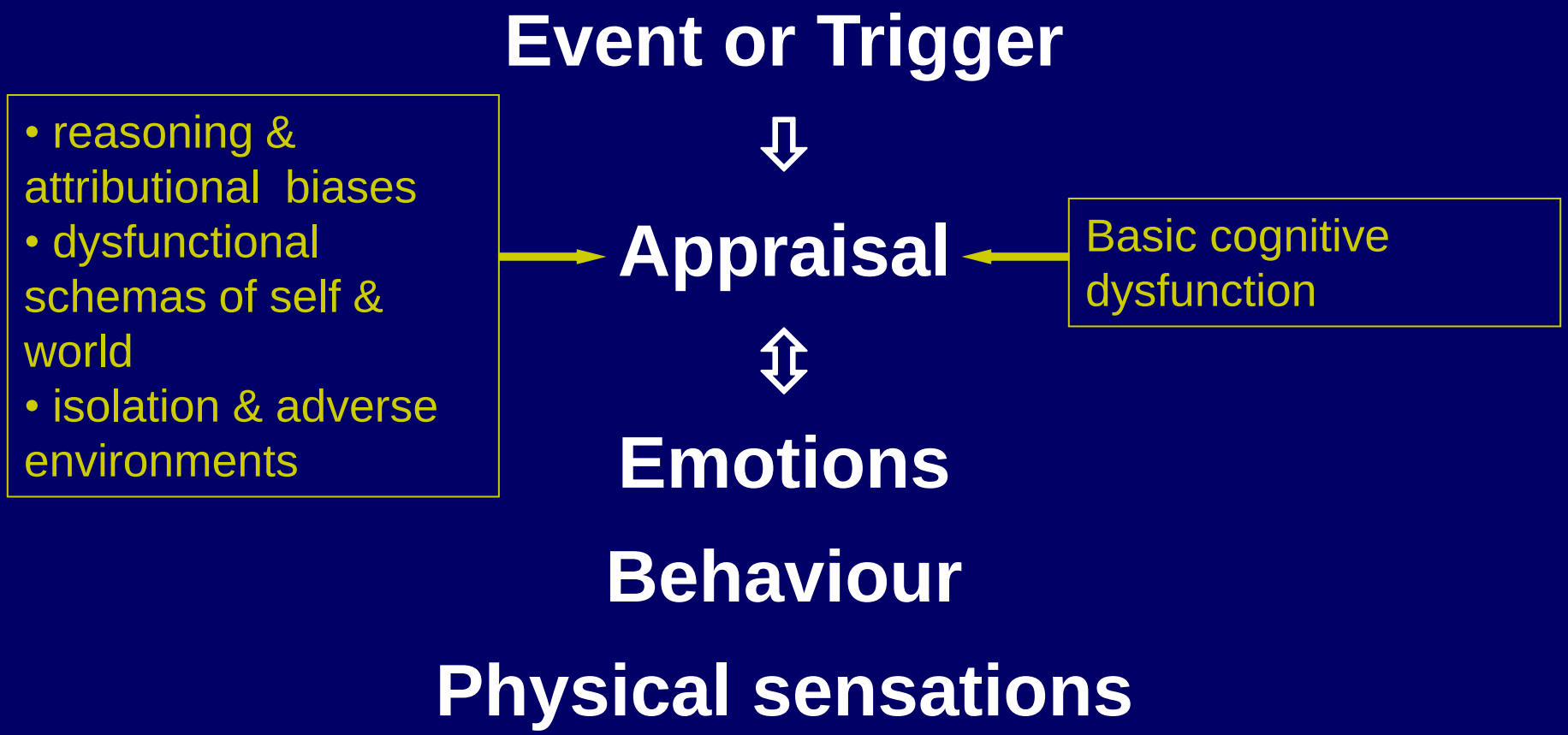
- Salience of information that might potentially enter awareness is influenced by dopamine, increased dopaminergic activity will result in attention being deployed inappropriately
- Inappropriately salient intrusions intrude into awareness.
- poor contextual integration and decrease in the influence of temporal context on attentional control.
- Thus, theories implicating impaired contextual integration and abnormal appraisal on the one hand and dopamine dysregulation on the other may be attempts at explaining the same processes at the different levels of information-processing and neurochemistry respectively.

Cognitive biases and delusion formation in the at-risk mental state

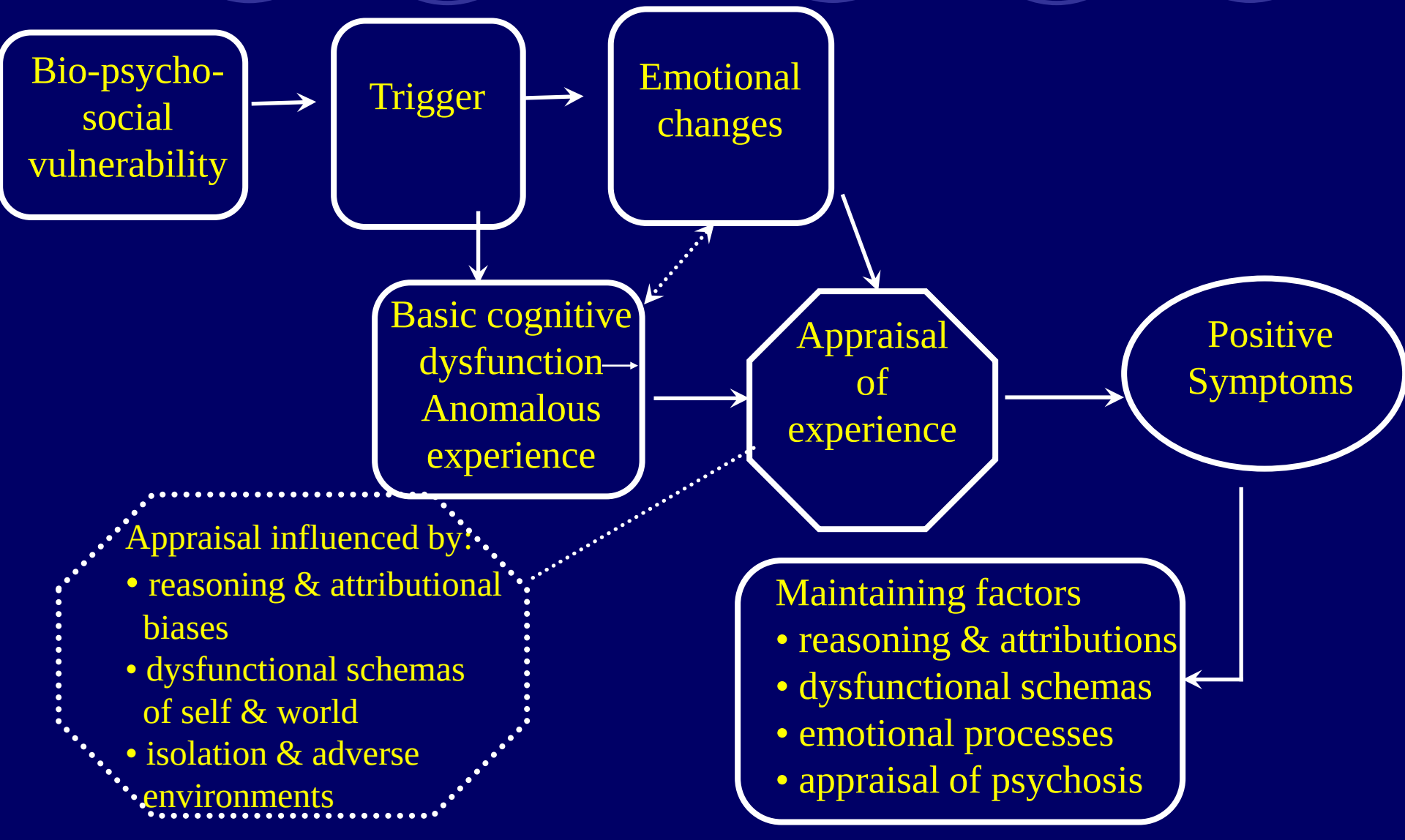
Reasoning biases and anomalous experiences

- Crucial role of appraisal of experience in onset of psychosis.
- Cognitive model of psychosis
- Reasoning bias: data from at-risk group
- Correlations with bias in this group.

Cognitive Model



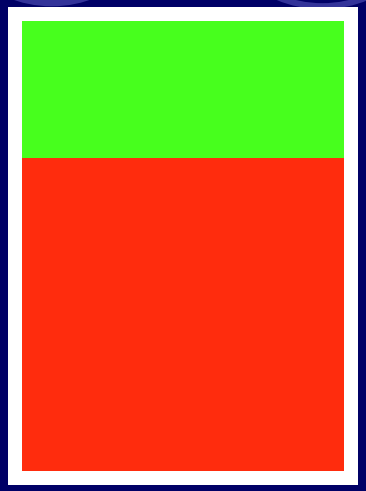
A Cognitive Model of the Positive Symptoms of Psychosis (Garety et al 2001)



Data Gathering Bias in ARMS (1)

- ‘jumping to conclusions’ style of thinking in patients with delusions in context of schizophrenia
- Data gathering bias – reach decision with less evidence.
- Beads task

Jumping to conclusions



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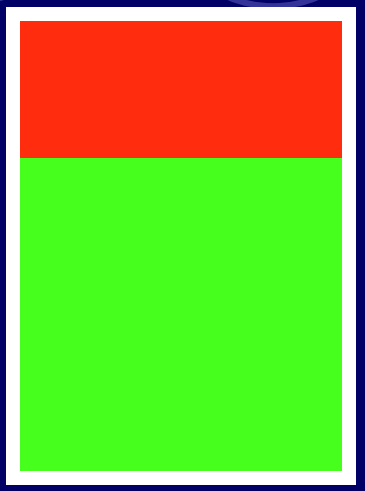
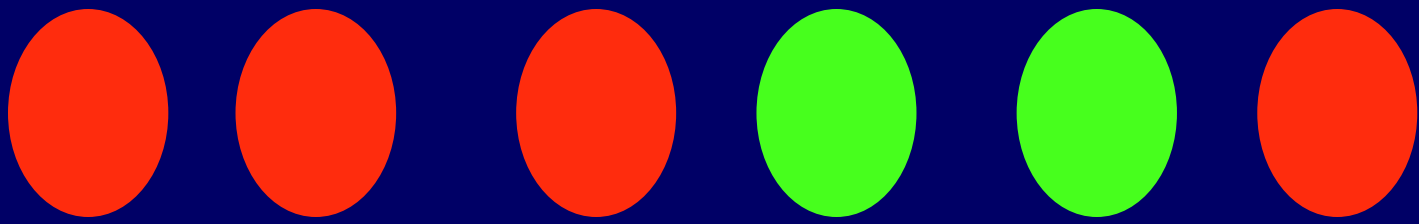




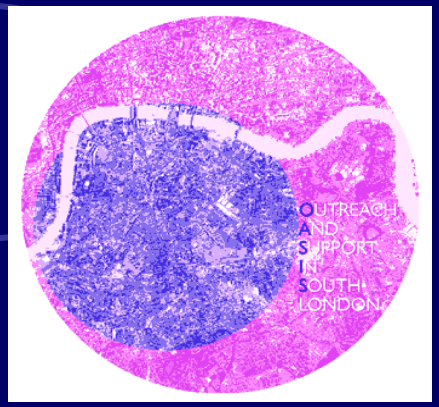
Which jar are the beads coming from?

Data gathering bias in ARMS (2)

- ARMS useful group: actively experiencing anomalous experiences but not fully psychotic or deluded.
- Hypothesis a): data gathering bias predates onset of delusions
- Hypothesis b): such a bias is related to either working memory dysfunction or personality style

OASIS

(Outreach And Support in South London)



- Outreach service for people (14-35 yrs old) with ‘at risk’ symptoms
- Primary Care setting (improve access & avoid stigmatisation)
- Designed to
  - Reduce ‘at risk’ symptoms and disability
  - Prevent transition to psychosis
  - Improve outcome if psychosis develops

Typical ‘prodromal’ signs

- ‘Attenuated’ psychotic symptoms
- Recent decline in function
- Depressive and anxiety symptoms

- Very high risk of psychosis:
  40% within 12 months

Data Gathering Bias in ARMS – measures/tasks

- IQ – Quick and NART
- Peters Delusion Inventory (PDI)
- Computerised version of beads task 85:15, 60:40, 44:28:28.
- Pseudo-random play-list.
- Jars of beads used in explaining task.
- Psychopathology in ARMS included PANSS, Ham-A, Ham-D, Young's Mania Scale, SAPS delusion subscale.
- Kruglanksi Need for Closure
- Freeston Intolerance of Uncertainty

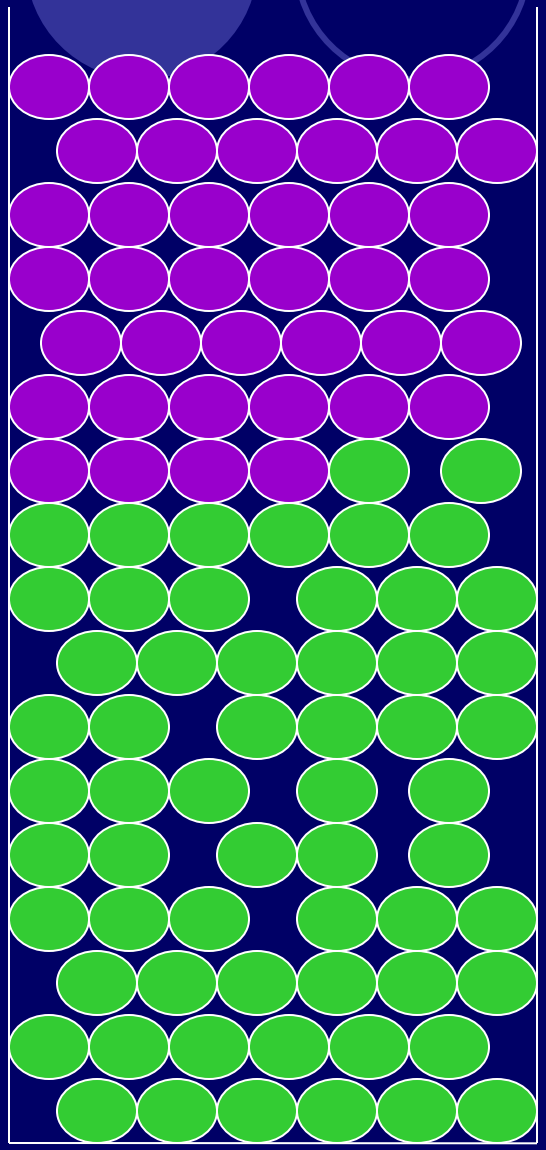
Methods

- ‘Memory beads’ – hopefully analogue of digit span.
- 10 trials of strings of beads to recall – differing length (5-9) and containing beads of different colours.
- Errors and span.
- ‘n-back’ – 0-back: attention, 2-back: working memory.

Data gathering bias in ARMS: Results I - demographics

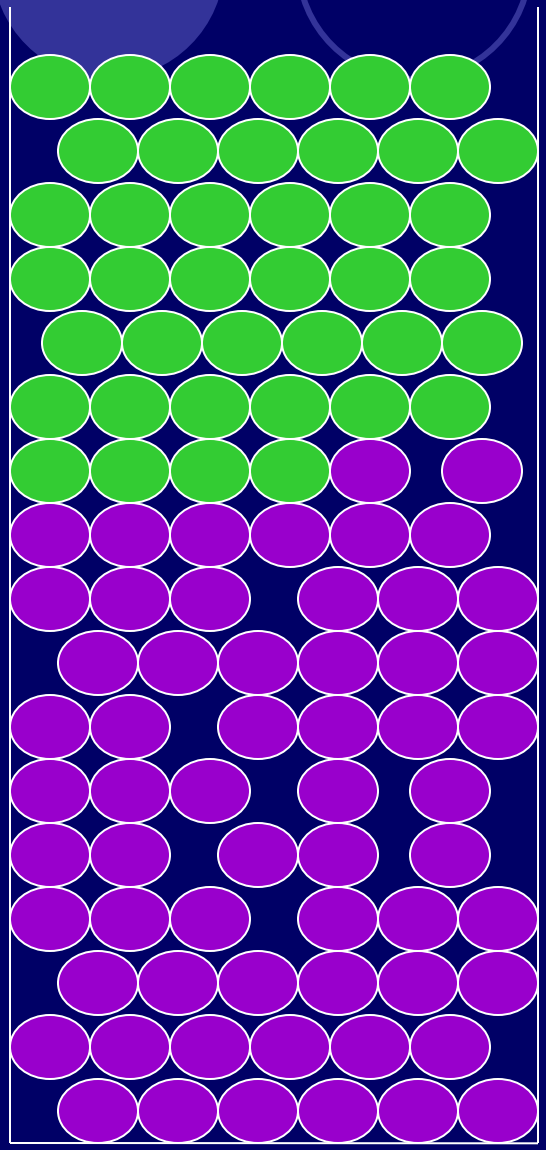
	Controls	ARMS
No. subjects	23	35
Age (mean)	25.1	24.2
IQ NART Mean (SD)	110.9 (3.0)	102.3 (4.3)

60 green
40 purple



(Mainly green jar)

60 purple
40 green



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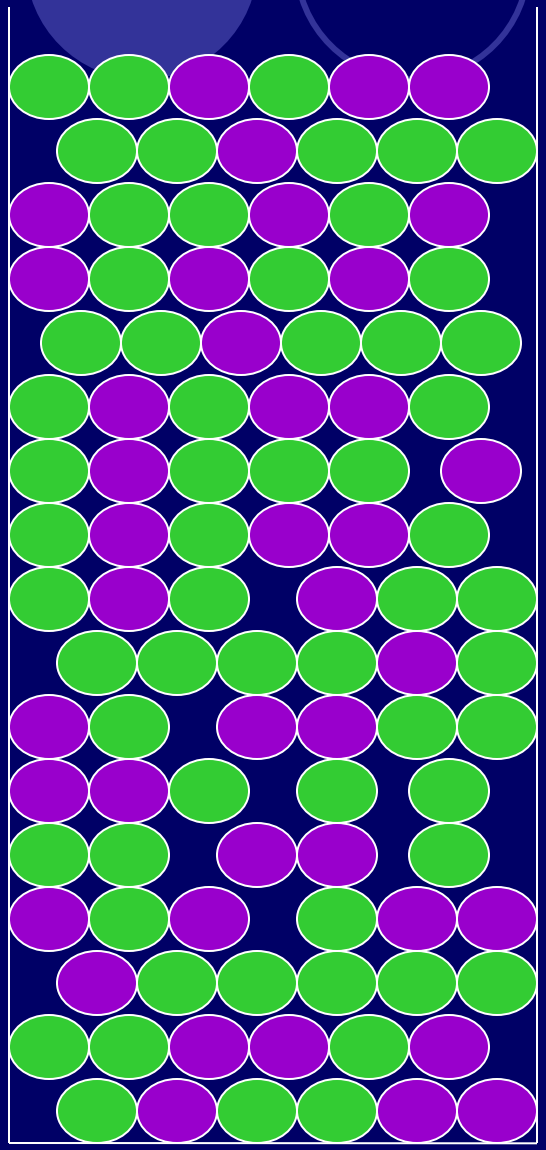

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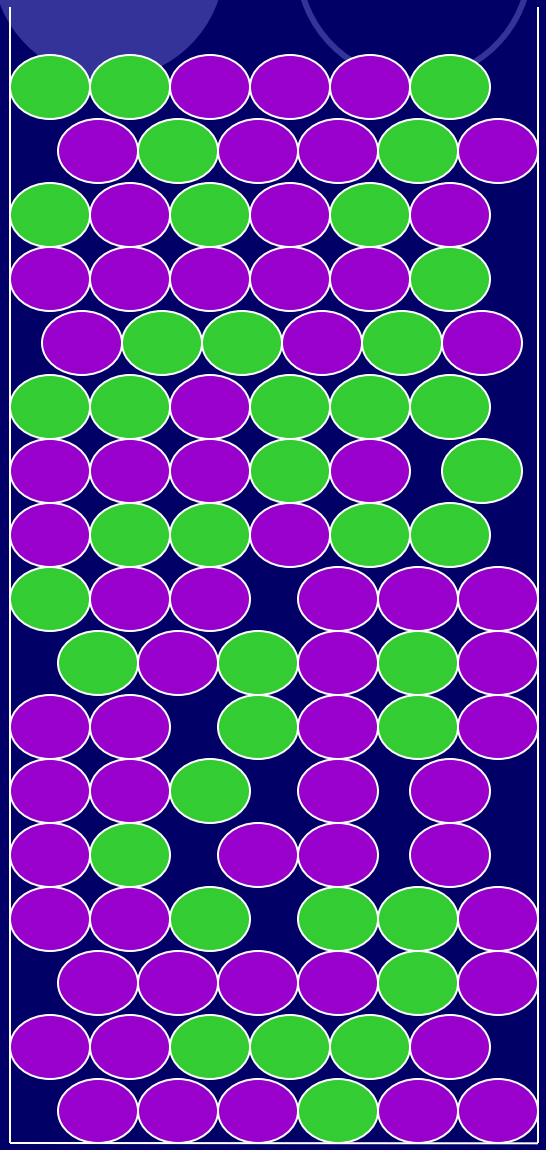
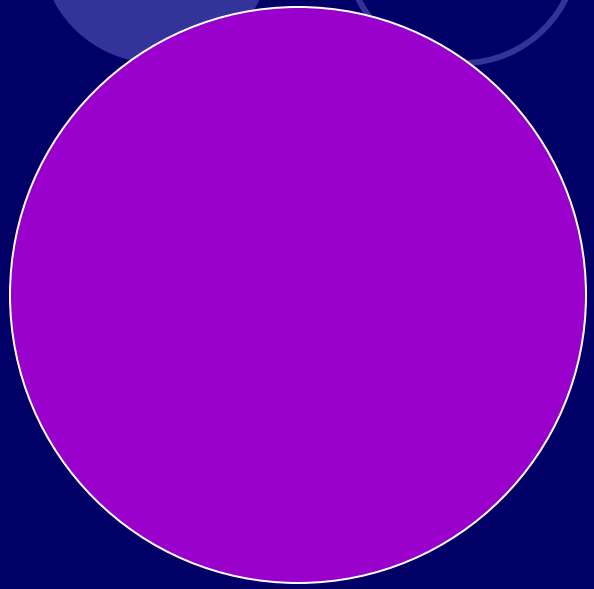


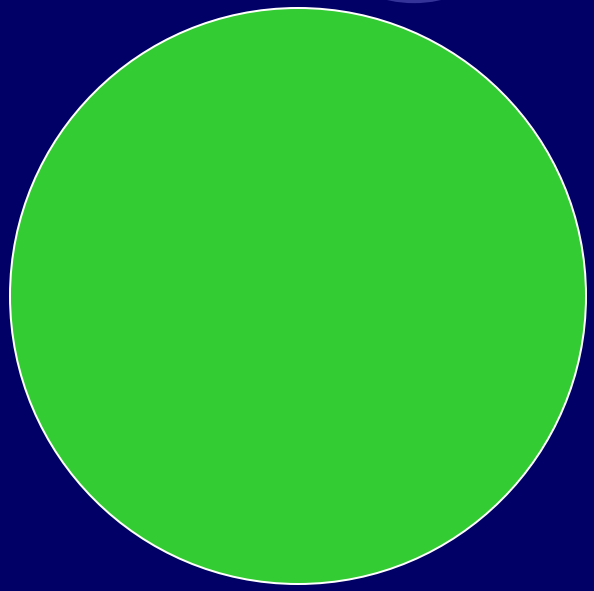
(Mainly purple jar)

The first bead is



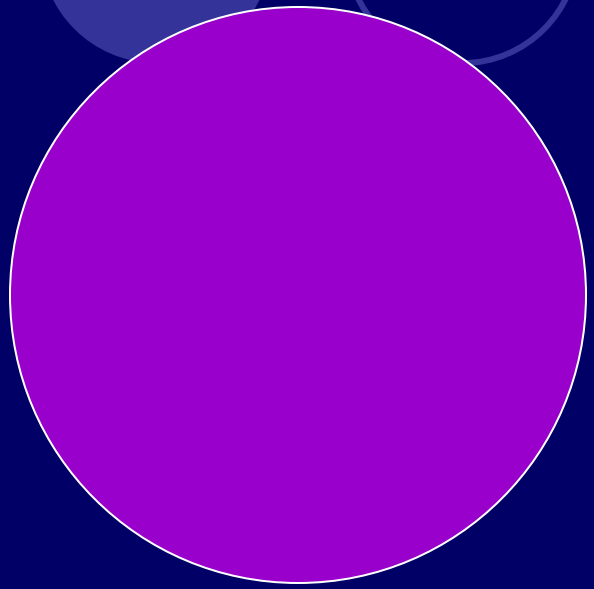
Do you want to see more beads or to decide now?

The second bead is



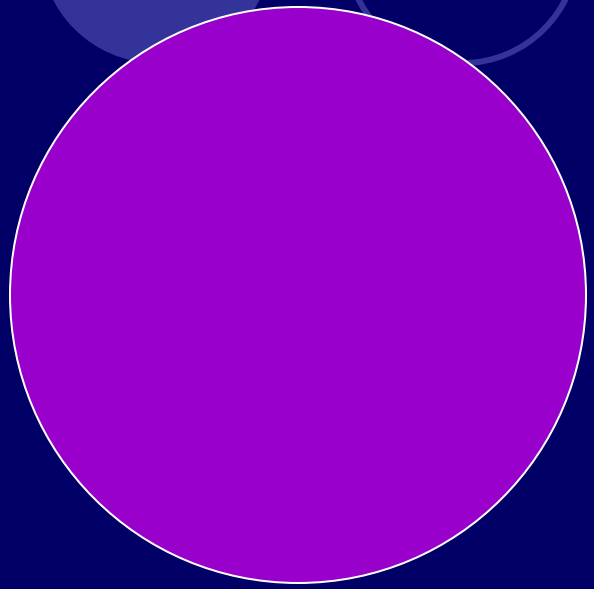
Do you want to see more beads or to decide now?

The third bead is



Do you want to see more beads or to decide now?

The fourth bead is

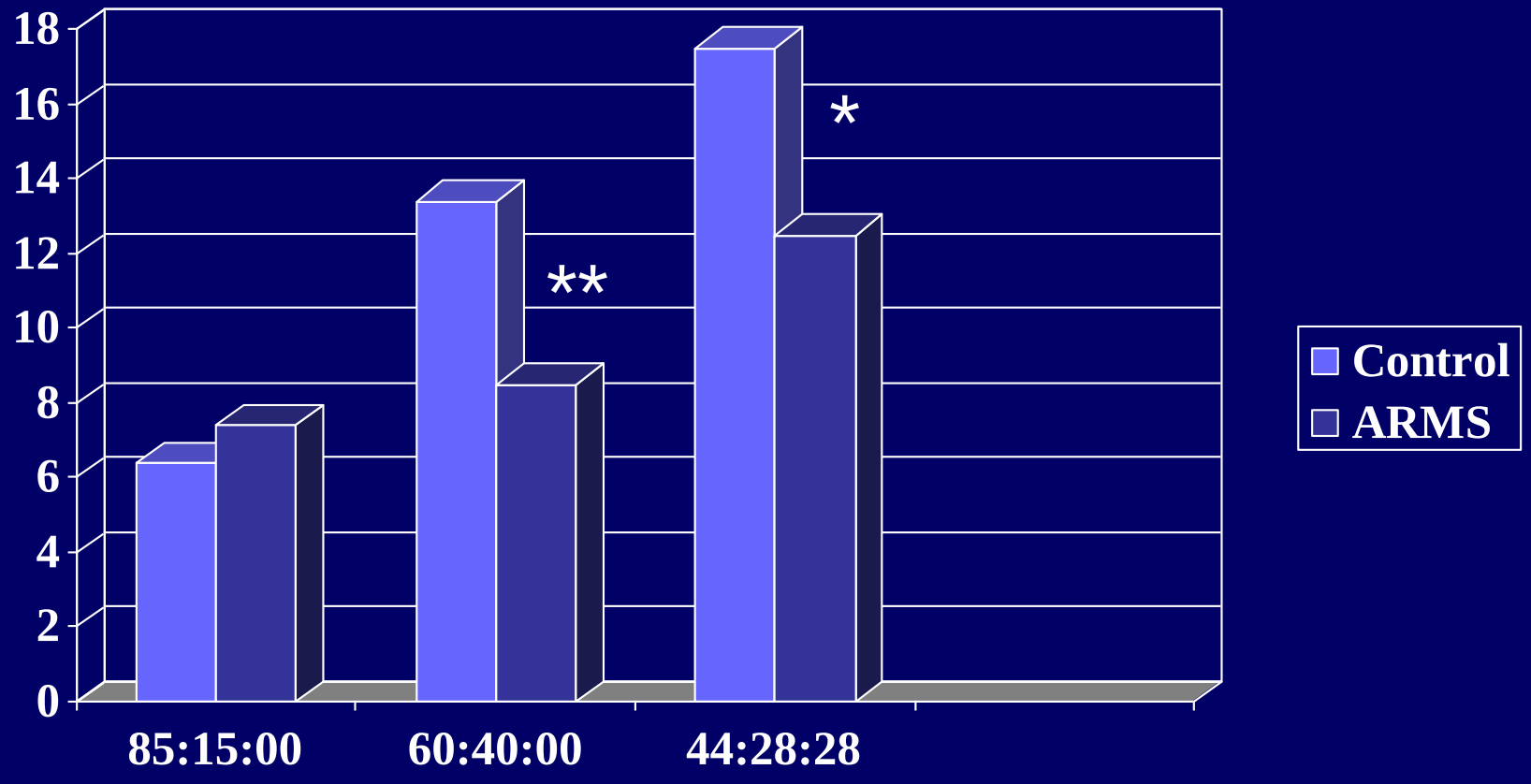


Do you want to see more beads or to decide now?

Data gathering bias in ARMS Results II – beads task

	Control	ARMS	Significant?
Easy (85:15)	6.4	7.4	N
Intermed (60:40)	13.4	8.5	Y – $p < 0.001$
Hard (44:28:28)	17.5	12.5	Y – p 0.012

Jumping to conclusions in the pre-delusional?



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Data Gathering Bias in ARMS (5) Results – PDI and personality traits

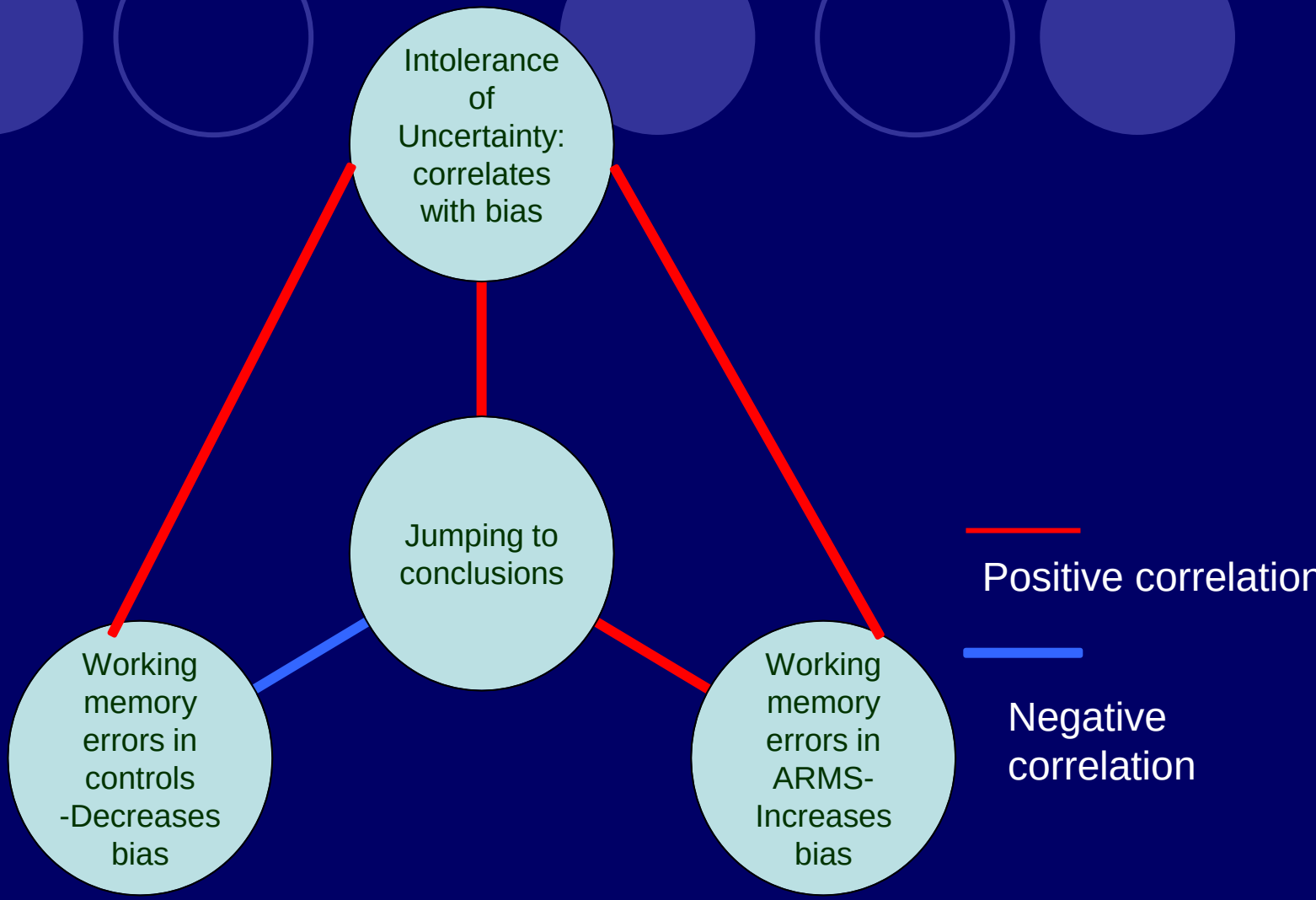
	Controls	ARMS	Significant
PDI total	**29.2**	**99.0**	**p < .001**
PDI distress	9.0	34.4	p < .001
PDI preoccupation	8.7	32.4	p < .001
PDI conviction	11.5	32.1	p < .001
NFC total	**10.9**	**11.6**	**NS**
NFC decisiveness	4.0	2.4	p= .019
NFC discomfort with ambiguity	4.3	6.0	p= .007
NFC closed mindedness	2.6	3.2	NS
Intolerance of Uncertainty	**58.3**	**80.8**	**p <.001**

Results - Correlations beads 60:40

PDI total	All subjects	-0.334	p=.019
PDI distress	All subjects	-0.282	p=.049
PDI preoccupation	All subjects	-0.331	p=.020
PDI conviction	All subjects	-0.373	p= .008
Intolerance of Uncertainty	All subjects	-0.285	p=.049
Memory beads	Controls	+ 0.444	p=.031
Memory beads	ARMS	- 0.451	p=.027

Conclusions

- Data gathering bias predates onset of psychosis and formation of delusions.
- Correlates with Intolerance of Uncertainty in both groups.
- Relationship with working memory differs in groups: memory error in controls leads to increased conservatism, in ARMS increased JTC bias.


Intolerance of Uncertainty: correlates with bias
Jumping to conclusions
Working memory errors in controls -Decreases bias
Working memory errors in ARMS-Increases bias
Positive correlation
Negative correlation

Summary

- Delusions are hard to define and heterogeneous but an essential part of what psychosis means and the criteria for the diagnosis of schizophrenia.
- Gradual merging of social, biological, and cognitive accounts of pathophysiology.
- Empirical data suggests that cognitive biases exist prior to onset of psychosis and development of delusions.

OASIS Clinical and Research Team and co-investigators

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