What is Autism and How to Make a Diagnosis

Dene Robertson
Where does the A come from?

Morel 1856: *Demence Precoce*  
Bizarre behaviour and mental function, withdrawal and self neglect

Kraepelin 1896: *Dementia praecox*  
Hallucinations, delusions, thought emotional blunting. Onset early adult life with "demented" end stage.

De Santis 1906: *Dementia praecoxissima*  
Very early onset.

Bleuler 1911: *Schizophrenia*  
Four As: autism, ambivalence, associations.
Dr Leo Kanner. (1894-1981)
Austrian born psychiatrist working in Baltimore, USA.

*Autistic disturbances of affective contact*
Nervous Child 1943; 2:217

Based on 11 children seen in an outpatient clinic since 1938.
Kanner 2

‘autistic disturbances of affective contact’

shortly after birth
profound lack of social engagement
echolalia, literalness, pronominal reversal
unusual responses to inanimate environment
difficulties with change
Dr Hans Asperger (1906-1980)
Paediatrician working in Vienna.

*Die Autistischen Psychopathen im kindersalter.*
(Autistic Psychopathy in childhood.)

Archive für Psychiatrie und Nervenkrankheiten 1944; 117:76-136
Asperger 2

1944 – Vienna

males only: “extreme version”
strong language and cognitive skills
interest in acquiring unusual knowledge
runs in families
ICD 10 Autism/DSM IV Autism

Early onset, plus:

1. Qualitative impairment of social interaction

2. Qualitative impairments in communication

3. Restricted/stereotyped patterns of behaviour, interests and activities
Reciprocal social interaction - 1 of:

(1) decreased eye-to-eye gaze, facial expression, posture and gesture to regulate social interaction;

(2) failure to develop peer relationships that involve a mutual sharing of interests, activities and emotions;

(3) a lack of socio-emotional reciprocity (impaired or deviant response to other people’s emotions/lack of modulation of behaviour according to social context/a weak integration of social, emotional and communicative behaviours).
(1) a delay in/lack of development of spoken language not compensated by gesture or mime;

(2) relative lack of a ‘to and fro’ quality in conversation;

(3) stereotyped and repetitive use of language or idiosyncratic use of words or phrases;

(4) abnormalities in pitch, stress, rate, rhythm and intonation of speech.
Interests/activities - 2 of:

(1) an encompassing preoccupation - content or focus/intensity and circumscribed nature;
(2) compulsive adherence to specific, non-functional, routine/rituals;
(3) stereotyped and repetitive motor mannerisms that involve either hand/finger flapping/twisting, or complex body movements;
(4) preoccupations with part-objects or non-functional elements of play materials;
(5) distress over changes in small, non-functional, details of the environment.
Clinical Characteristics-I

Social Deficits

Problems orientating to name
Difficulties with eye contact, gesture and expression
Lack of interest in other children/avoidance
Few friends
Difficulties sharing excitement
Not seeking or giving comfort
Clinical Characteristics-II

Communication deficits

Language delay without non verbal compensation
Limited social chat/two way conversation
Stereotyped, repetitive use of language
Reduced social and imaginative play
Clinical Characteristics-III

Restricted repetitive interests/behaviour

- Circumscribed interests
- Unusual preoccupations
- Rituals/compulsions
- Motor stereotypies
- Difficulties with change
- Sensory interests or sensitivities

Onset before 36 months
The ‘Autism Spectrum’ in ICD-10

Childhood autism
‘High functioning’ autism
Asperger syndrome
Atypical autism
PDD-other
PDD-unspecified
Which is it - CA, AS or HFA?

CA: language delay/cognitive delay

AS: no language/cognitive delay

HFA: standard diagnosis, IQ >70
DSM-5 Autism Spectrum Disorder

A. Persistent deficits in social communication and social interaction across contexts, not accounted for by general developmental delays, and manifest by all 3 of the following:
1. Deficits in social-emotional reciprocity
2. Deficits in nonverbal communicative behaviors used for social interaction
3. Deficits in developing and maintaining relationships

B. Restricted, repetitive patterns of behavior, interests, or activities as manifested by at least two of the following:
1. Stereotyped or repetitive speech, motor movements, or use of objects
2. Excessive adherence to routines, ritualized patterns of verbal or nonverbal behavior, or excessive resistance to change
3. Highly restricted, fixated interests that are abnormal in intensity or focus
4. Hyper-or hypo-reactivity to sensory input or unusual interest in sensory aspects of environment;

C. Symptoms must be present in early childhood (but may not become fully manifest until social demands exceed limited capacities)

D. Symptoms together limit and impair everyday functioning.
Comparison of ICD-10R, DSM-IV-TR and DSM-5 in an Adult ASD Diagnostic Clinic

Of those diagnosed with an ASD using ICD-10R

- 56 % met DSM-5 ASD
- 19 % met DSM-5 criteria Social Communication Disorder
- Roughly 25% lost diagnosis completely

Of those diagnosed with Autistic Disorder/Asperger Syndrome on DSM-IV-TR 78 % met DSM-5 ASD criteria

Prevalence

Ehlers and Gillberg (1993): 0.4 – 0.77% aged 7 to 16 years M/F = 4:1

Scott et al (2001): 0.6 % Broader phenotype age 5-11 years M/F 4:1.

Fombonne et al (2005): Broader phenotype in adults: 0.6%

Brugha et al (2012): Adults: 1.1% (0.3-1.9). M/F = 6:1

More common with decreasing IQ
Prevalence of ASD in General Psychiatry OPD

• Small number of studies suggest between 0.6% and 1.4% in general psychiatry out-patient clinics for adults

• Measured using Screening Instrument (Autism Quotient, Baron-Cohen et al. 2001)

• Screening Instruments may not be valid in non-native populations - cut-off points?

• Not clear how well screening instruments can differentiate from co-morbidities e.g. schizophrenia
Possibly indicative of undiagnosed ASD

- Inexplicable violence
- Computer crime
- Offences arising out of misjudged social relationships
- Obsessive harassment (stalking) (Berney, 2004)

5 types of ‘stalker’ (Mullen et al, 1995):

‘Incompetent suitor’ characterised by:
Isolated
Lonely
Socially inept.
Typically male, underemployed, average intelligence.
Genetics

Not Mendelian, polygenic:  
- MZ:DZ = 60:3-5% concordance for strict phenotype:
- Heritability ~ 90% (family/twin studies)
- Relative risk to sibling ~5-20x

Candidate gene assoc. studies:
- MET: Tyrosine kinase
- SLC6A4: Serotonin
- RELN: Neuronal migration
- TSC1,2 PTEN: Tumour suppressors
- Neuroligins/Neurexins: Cell adhesion

Endophenotype approaches:
- Phenotypic markers may segregate independently (eg age at first words to Ch 7)
Copy Number Variations

- Small deletions or duplications
- 40,000 oligonucleotide probes printed on slide
- Pt DNA labeled and hybridised
- Part of normal genetic variation (55,000 reported)
- Some give rise to disease
  - Prada-Willi/Angelman del 15q11-13
  - MECP2 dup Xq28
  - VCFS del 22q11.2
- In large samples, some CNVs more frequent in disease cases than controls
- Autism: >7% – increased probe resolution may uncover more.
Conceptualising Autism

1. Theory of mind
2. Executive Function
3. Central coherence.
Theory of Mind

Attribute mental states to self and others to predict/explain actions

Experimental tasks - differing levels of complexity

Not all people with autism fail ToM tasks

Mentalising deficits may spring from a more primary deficit

Explains impairments in social interaction but not all the features of autism

Baron-Cohen, Leslie and Frith (1985)
Executive Function

Goal-oriented, purposive behaviour

Volition
Planning
Purposive Action
Self-Regulation: productivity and flexibility
Executive Function - ASD

- More likely to make perseverative errors on the WCST
- Significantly reduced fluency (word & design)
- Impaired performance on spatial working memory tasks
- Can account for a range of features including repetitive behaviours & concrete thinking
Central Coherence

Information processing - normal tendency to perceive patterns/objects as ‘wholes’

**Autism:** better performance on tasks which require preferential processing of parts over wholes e.g. Block Design and Embedded Figures (Shah and Frith, 1983)

Frith (1989) - ‘Weak Central Coherence’
Central Coherence - ASD

Could account for:  rote memory
                  preoccupation with parts of objects etc.

Similar findings in schizophrenia

Anxiety may play a role in narrowing attention
How to make a diagnosis...

Need informant!

Interaction/communication/special interests

Preferred routines

Cognitive profile/theory of mind

Interpersonal history/history of bullying

Comorbidity
Semi-standardised tools:

• **Autism Diagnostic Interview - Revised**
  Clinician administered
  Parents/caregivers in first 5 years of life
  Less reliable with adults (ADI; Lord, 1994)

• **Autism Diagnostic Observation Schedule**
  Clinician interview/observation of patient
  Adults or children (ADOS; Lord et al, 1999)

Many others + screening instruments (eg ASQ)
<table>
<thead>
<tr>
<th>Subject's name:</th>
<th>NHS number:</th>
<th>Interviewer's name:</th>
</tr>
</thead>
<tbody>
<tr>
<td>Subject's date of birth:</td>
<td>Subject's age:</td>
<td>Date of Interview:</td>
</tr>
</tbody>
</table>

Names of informants (and their relationship with the subject):
About this guide

This interview guide provides probes to help clinicians in making a diagnosis of ASD in adults (including Asperger Syndrome / High Functioning Autism) using the criteria in ICD-10 (F84) or DSM IV (299). This guide is not suitable for assessing adults with a substantial learning disability.

The guide is:
- only a guide and, with experience, clinicians will adapt it to their own style of interviewing. Initially, clinicians should stick to the suggested probes
- a clinical tool to help clinicians to gather the relevant information, organise it and then come to a clinical judgement about someone who has reasonably clear-cut ASD (i.e. it does not include an algorithm)
- set out to enable the clinician to make notes in the appropriate domain (as one probe may trigger a response in another domain)

The guide is not:
- adequate for someone with a more subtle form of disorder who will need to be assessed by someone familiar with the condition and who may be using longer and more extended interviews
- designed to gather information which is not immediately relevant to the diagnosis (e.g. sensory anomalies, symptoms of ADHD or psychiatric illness)

Using this interview guide

It is essential to find out how the subject functions outside the clinic, as well as in earlier life. Information from informants (e.g. parents) who knew the subject in the past or in the community is very important.

Informants and Subjects

The guide uses two typefaces:
- Standard typeface: Suggested probes for interviewing the informant – someone who knows the subject very well (e.g. relative/friends/support worker)
- *Italic typeface: Suggested probes for interviewing the subject*

Important notes

- ASD distorts the presentation of comorbid psychiatric disorder, making it more difficult to detect (e.g. depression can be masked by the subject’s difficulty in describing his/her internal feelings or an inappropriate facial expression)
- in talking about social relationships or feelings, some people may recite answers that appear excellent, but may have little real understanding of the underlying meaning/emotion
- the probes are suggestions rather than precise questions and may lead to further discussion in any area
- keep checking as to how the subject was in the past (particularly in childhood) as well as how (s)he is now and when the symptoms were first noticed
- ask whether a symptom bothers anyone else (i.e. the people they are living with) as individuals often do not appreciate the extent to which their behaviour is unusual
- get concrete examples of behaviour rather than general descriptions
Tell me about the schools you were at.
- how did you get on with people there?
- did you enjoy being with people?
What about at work/college?
Tell me how you get on with people?
- any problems in the past /now?

Tell me about the sort of things that people do that annoy/irritate you.
- do you do things that annoy other people?
Tell me about teasing/bullying (is it something you’ve been involved in?)
- how does someone stop being teased/bullied?
Do you feel different to other people in any way?

How good are you at understanding what other people say or do? (where they are coming from?)
Tell me about times when there’s been a problem because you didn’t understand something.

How good are you at picking up what someone is feeling?
- for example, what do you do if someone is obviously sad? (how would you try to comfort them?)
Area 2: Communication

How I would like to go into how <Name> communicates – both in the present and how (s)he has developed from childhood.

LANGUAGE DELAY  Any evidence of early language delay? Normally children use single words by 24 months and short phrases by 33 months.

When did <Name> start to speak?
- first meaningful use of words (other than ‘mummy’ or ‘daddy’)
- first use of meaningful (not echoed) phrases
Did (s)he ever see a speech therapist?
Was anything about his/her early speech unusual?
Did anyone suggest that (s)he might be deaf?

Tell me what you know about how you learned to talk.
- Has anyone ever said that you were late talking?
When you first went to school, did other people have any difficulty in understanding what you said?

Have you ever seen a speech therapist (if so, why)?

UNUSUAL SPEECH  Any evidence of the unusual speech that is characteristic of ASD?

Is the way <Name> talks peculiar or unusual in any way (compared to peers or siblings)? i.e.
- monotonous, an odd tone of voice
- too fast/slow, too quiet/loud
- unusually formal or pedantic
- using odd words/phrases
- using ‘pet’ phrases
- unusually repetitive

When you were a child, did people ever comment on the way you spoke?
- compared to the other children around you, were you any different?

Suggested probes for interviewing the subject
Area 3: Rigidity (and focal/repetitive interests)

**RIGIDITY**

The extent to which rigidity is a characteristic – to the degree that the subject has difficulty in coping with unexpected change.
- the extent to which (s)he is a slave to a routine or to some ritual.

Has <Name> had any unusual, set routines that interfere with everyday life?
- how did (s)he cope if they had to be changed?
- and with something that was unexpected?

How organised a person are you? Are there things you like to do a certain way or to a set routine?
- have you ever had set routines?
- what happens when you can’t do things in the way you would like (or when you have to change your plans)?

Has <Name> had any unusual behaviour (stereotypies/mannerisms)? For example when (s)he has been stressed, excited or trying to calm down?
- e.g. has (s)he flapped, twiddled, or played with things or rocked?

**HOPES FOR THE FUTURE**

Where do you see yourself in five years time?

**Suggested probes for interviewing the subject**
### Observation

It is possible, besides the interview, to see the subject in a less formal setting e.g. collect him/her from the waiting room where characteristics are often more prominent.

**SOCIAL INTERACTION**  The extent to which the subject comfortably mixes with, and relates to, other people

<table>
<thead>
<tr>
<th><strong>COMMUNICATION – SPEECH</strong></th>
<th>The extent to which:</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>the speech sounds normal – note whether it has an unusual tone, stress, pitch, rate, rhythm or volume</td>
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<tr>
<td></td>
<td>the tone of the voice reflects the subject’s emotional state</td>
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<tr>
<td></td>
<td>he/she is able to engage in a conversation, taking turns at the appropriate point</td>
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<tr>
<td></td>
<td>he/she appreciates how much/little information the hearer requires to make sense of what is being said</td>
</tr>
<tr>
<td></td>
<td>speech is unusually formal / pedantic</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th><strong>COMMUNICATION – NON-VERBAL</strong></th>
<th>The extent to which:</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>facial expression is varied, communicative and vivacious</td>
</tr>
<tr>
<td></td>
<td>eye contact is natural and expressive and is used to reinforce what is being said</td>
</tr>
<tr>
<td></td>
<td>gesture is used and whether it is:</td>
</tr>
<tr>
<td></td>
<td>emphatic (e.g. beats of the hand)</td>
</tr>
<tr>
<td></td>
<td>conventional (e.g. clapping, hand over the mouth)</td>
</tr>
<tr>
<td></td>
<td>informational</td>
</tr>
<tr>
<td></td>
<td>(e.g. nods and shakes of the head, shrugs, pointing)</td>
</tr>
<tr>
<td></td>
<td>descriptive (e.g. showing the shape or size of something)</td>
</tr>
</tbody>
</table>

### Appearance

- Any unusual stereotypies (e.g. hand flapping, finger twiddling, or rocking)
- Anything else that seems unusual/ eccentric
## Assessment outcome and next steps

<table>
<thead>
<tr>
<th>EVIDENCE IN SUPPORT OF A DIAGNOSIS OF ASD</th>
<th>IMPACT ON FUNCTIONING (both on the subject and on others)</th>
</tr>
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<tbody>
<tr>
<td>Reciprocal social interaction</td>
<td></td>
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<tr>
<td>Communication</td>
<td></td>
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<tr>
<td>Rigidity (and focal/repetitive interests)</td>
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### ASSESSMENT OUTCOME AND NEXT STEPS

- **Diagnosis**
- Referral for further assessments and plans for intervention and care
Differential Diagnosis

• Schizophrenia
• Schizotypal disorder
• Schizoid PD
• Anankastic PD
• OCD
• Learning disability
What we do (BGC)...

- Pre-Assessment self and observer rating reports
- ADI-R +/- ADOS (preferably both)
- Psychiatric Interview with particular attention to Developmental History
- Psychosocial functioning
- Co-morbidity
- Physical exam
- Consensus Clinical Opinion
- Neuropsychology?
- Imaging?
- Genetic testing?
In our clinic:

Of all patients seen 43% received a diagnosis of an ASD
BGC: Where on the Spectrum?

% of Patients Diagnosed

- Asperger's Syndrome (n = 55)
- Childhood Autism (HFA) (n = 41)
- Atypical Autism (n = 39)
- PDD-NOS (n = 15)
Can We Predict ASD Using Whole Genome Association Data?

<table>
<thead>
<tr>
<th></th>
<th>Total Sample (n)</th>
<th>Predicted (n)</th>
<th>Accuracy (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>ASD Affected</td>
<td>1385</td>
<td>1264</td>
<td>91.3</td>
</tr>
<tr>
<td>Unaffected</td>
<td>1494</td>
<td>1253</td>
<td>83.9</td>
</tr>
<tr>
<td>Total</td>
<td>2879</td>
<td>2517</td>
<td>87.6</td>
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Accuracy = 88%
Specificity = 84%
Sensitivity = 92%
Morphometric diagnosis?

Cortical thickness
Convexity
Distortion
Pial area
(Radial curvature)

Red: ASD > controls

Catatonia in ASD

Motor disorder: stereotypy, rigidity, mutism, posturing
Increased slowness in movement and verbal response
Difficulty in action initiation and completion
Increased reliance on prompts
Increased passivity/decreased motivation

In ASD many children have some features from early childhood

Some develop catatonia-like regression as youths/adolescents
(Wing and Shah, 2000)
Catatonia in ASD (2)

- Rarely progress to full stupor and most make gradual improvement
- 3 studies: 800 children, adolescents, and young adults
- 6–17% had catatonia-like deterioration
- Worsening symptoms associated with stress
- Is there a sub-group of ASD with Catatonia? (Dhossche, 2004)