Psychiatric comorbidities in ASD

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Prevalence

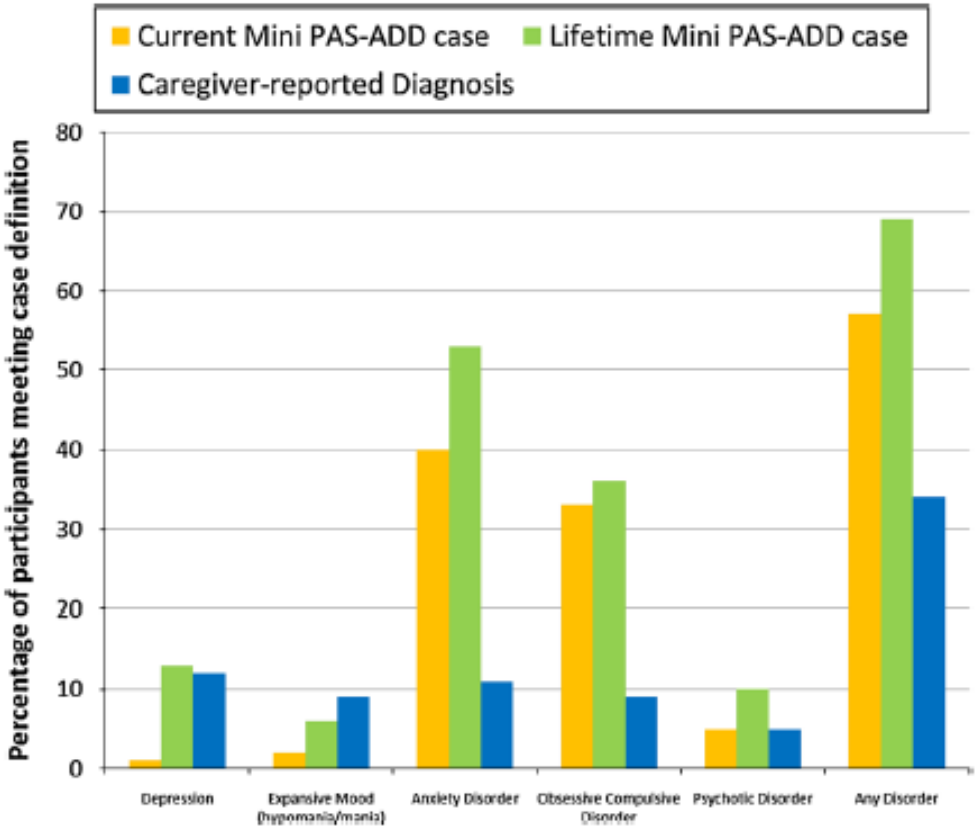


Fig. 1 Percentages of participants with a psychiatric disorder based on caregiver-report, current and lifetime Mini PAS-ADD criteria

However, mush lower rates of both anxiety and depression in those with ID

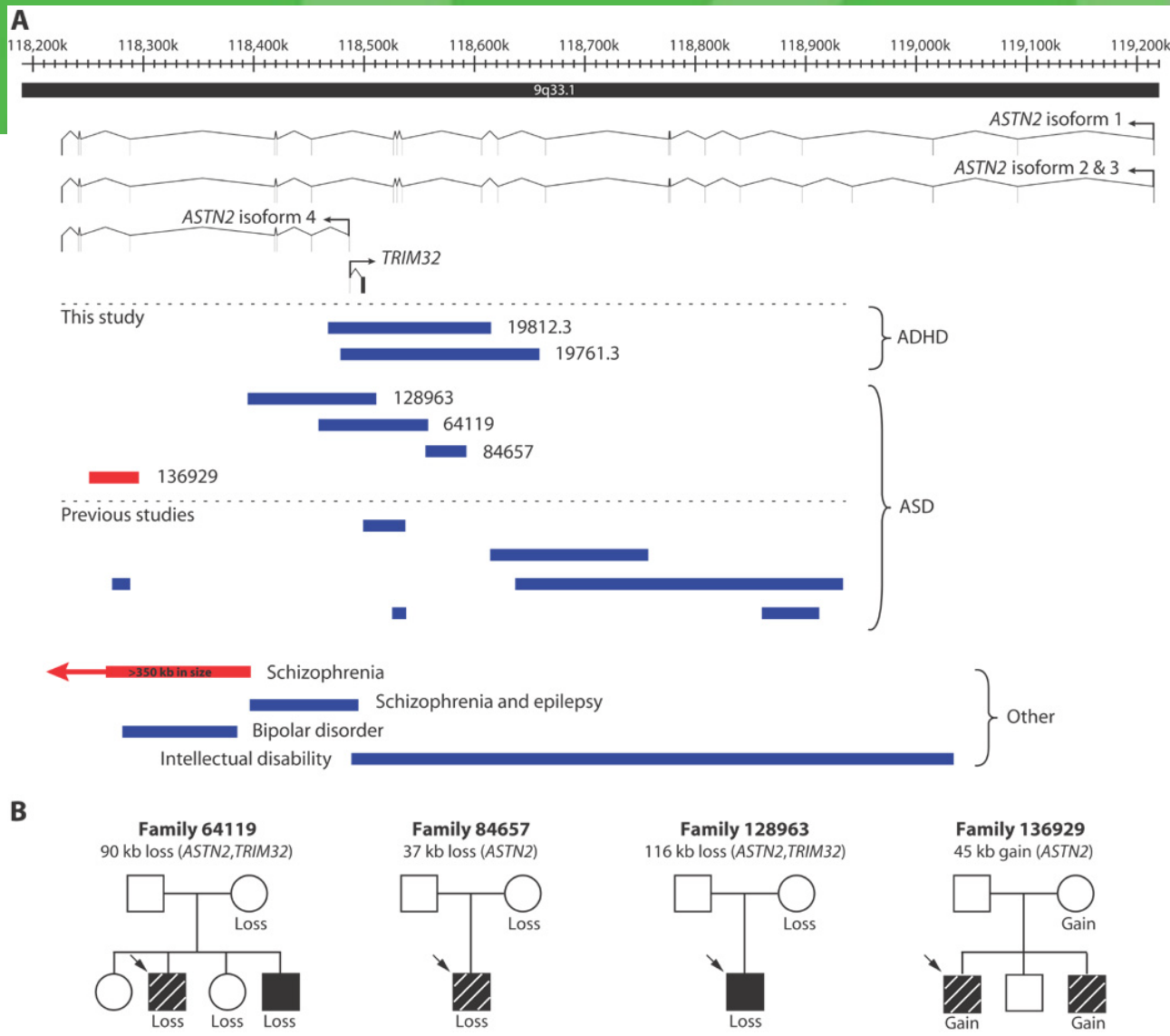
Buck et al, 2014

Questions raised by high prevalence

- High co-occurrence of several neuropsychiatric conditions, more than expected from general population rates

- Do our diagnostic constructs map onto distinct biologic constructs
- Is there construct confusion, from measurement point of view
- What does it mean of treatment development

- Do our diagnostic constructs map onto distinct biological constructs?



Most common phenotypes: ASD, ADHD, ID, language delay, anxiety, OCD

Lionel A C et al. Sci Transl Med 2011;3:95ra75-95ra75

Is there construct confusion, from measurement point of view

- How do we make diagnoses about internalizing disorders in the context of limited reporting of subjective experiences
  - E.g. is a diagnosis of anxiety made based on observable behavior the same construct as a diagnosis of anxiety made based on self report of internal states
  - Can biology clarify that question

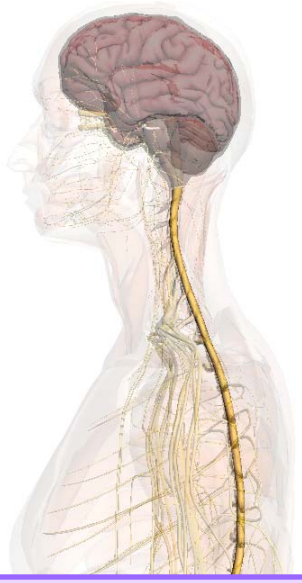
ANS Response To Anxiety

Well-documented in typically-developing individuals

Parasympathetic branch

"rest & digest" response

Decreases sweating
Decreases heart rate
Cutaneous vasodilation



Sympathetic branch

"fight or flight" response

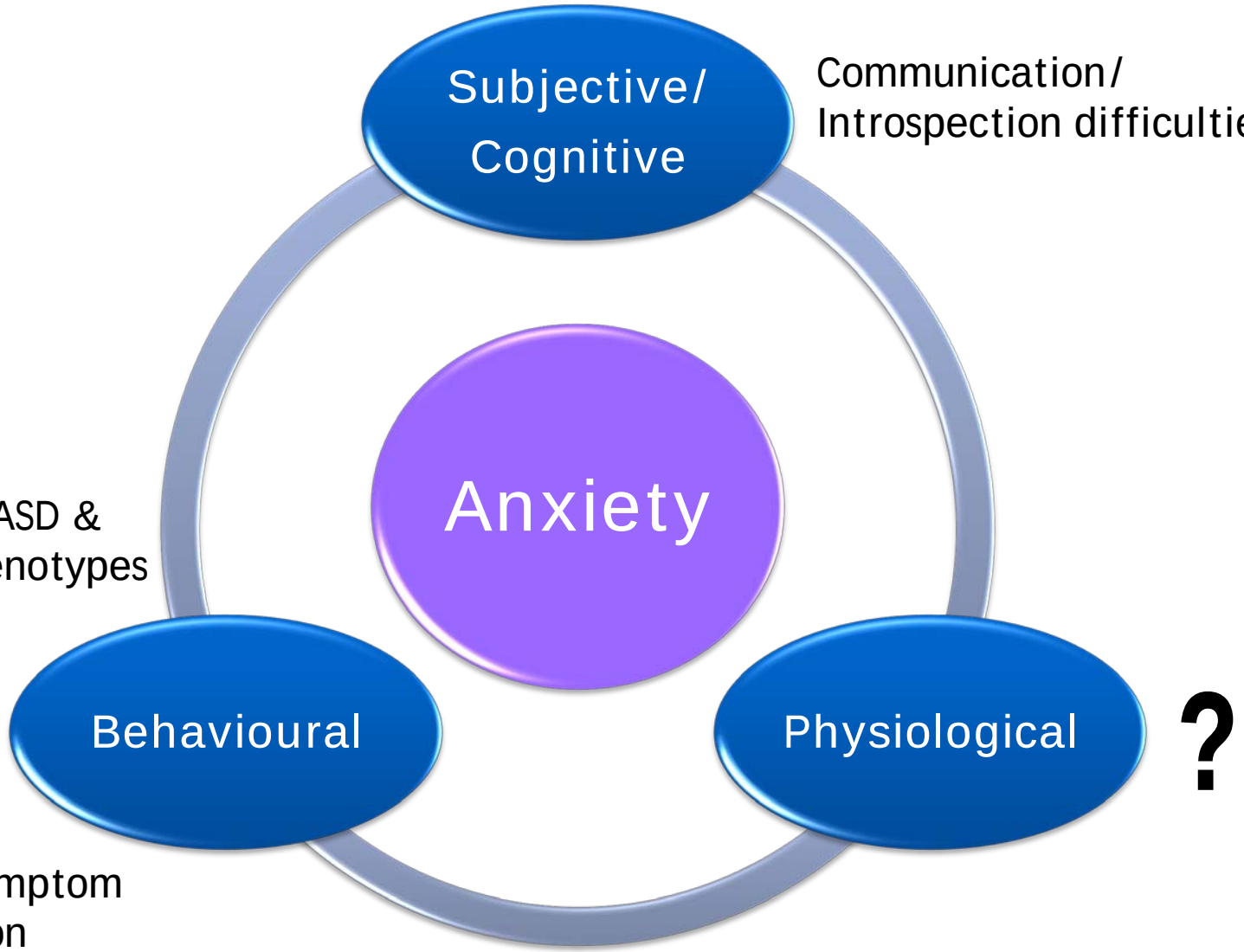
Increases sweating
Increases heart rate
Cutaneous vasoconstriction

- Electrodermal activity
- Cardiac activity

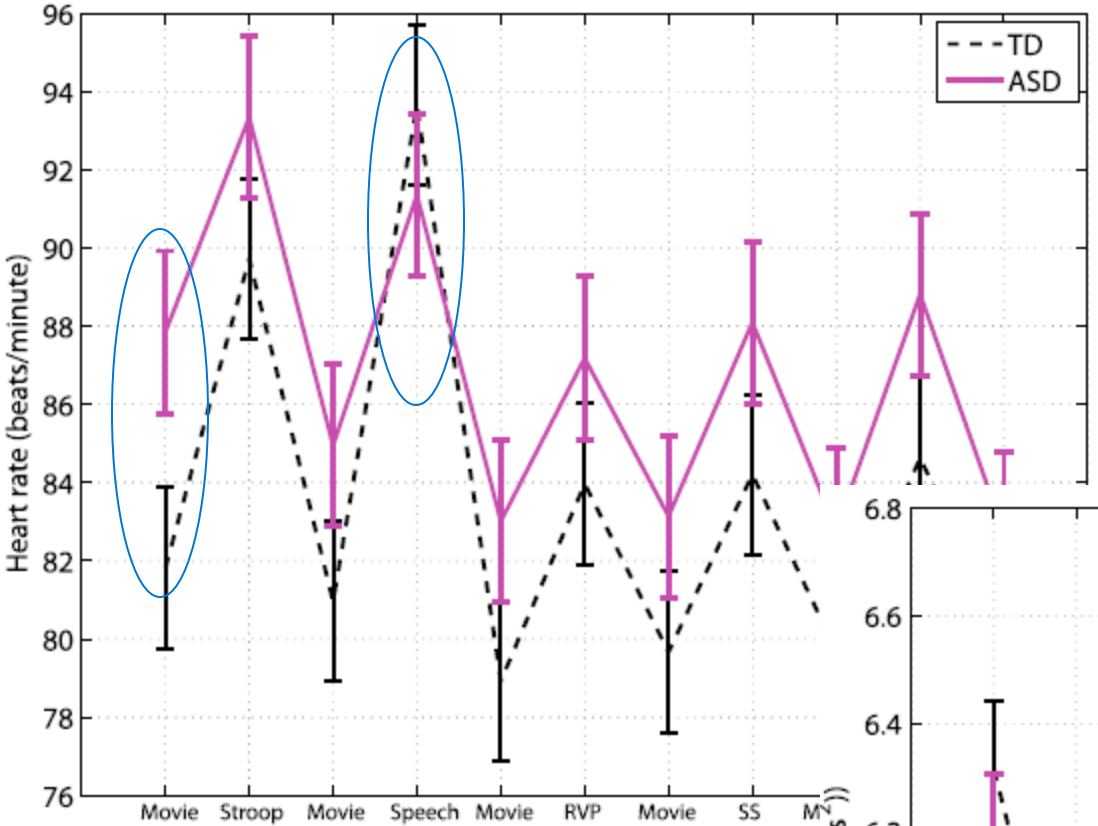
Source: Google Body

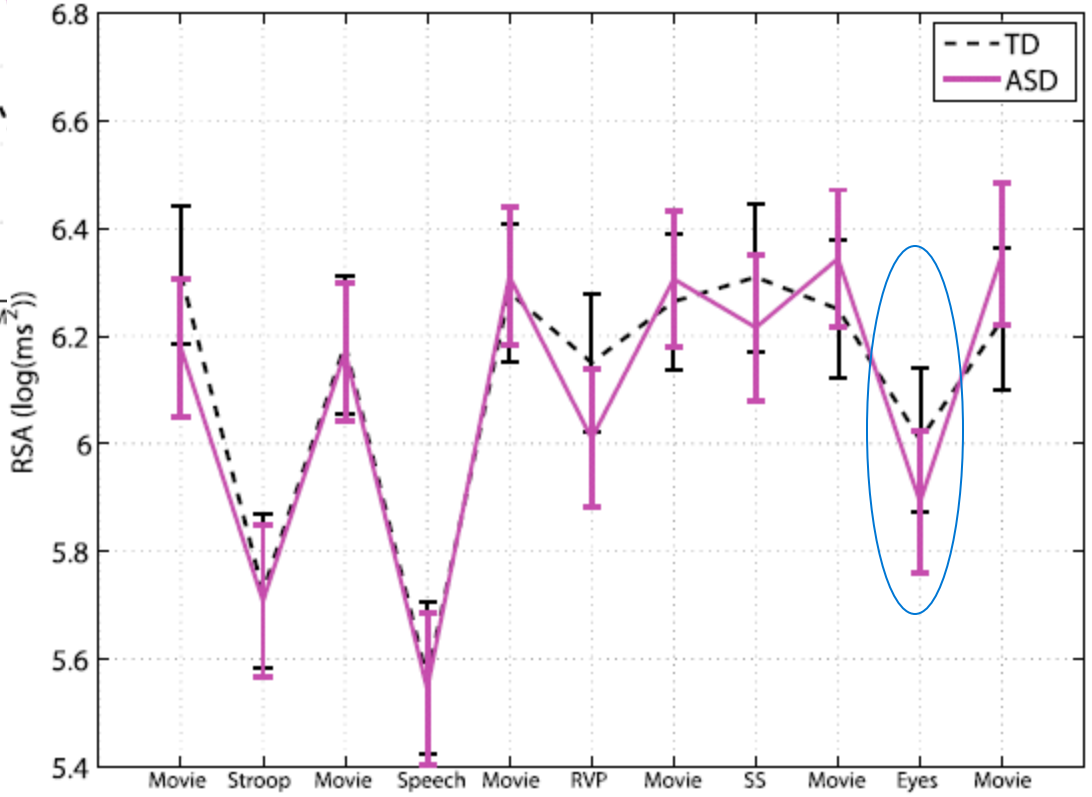
Tripartite Model of Anxiety (Lang, 1968)

Implications for assessment & treatment



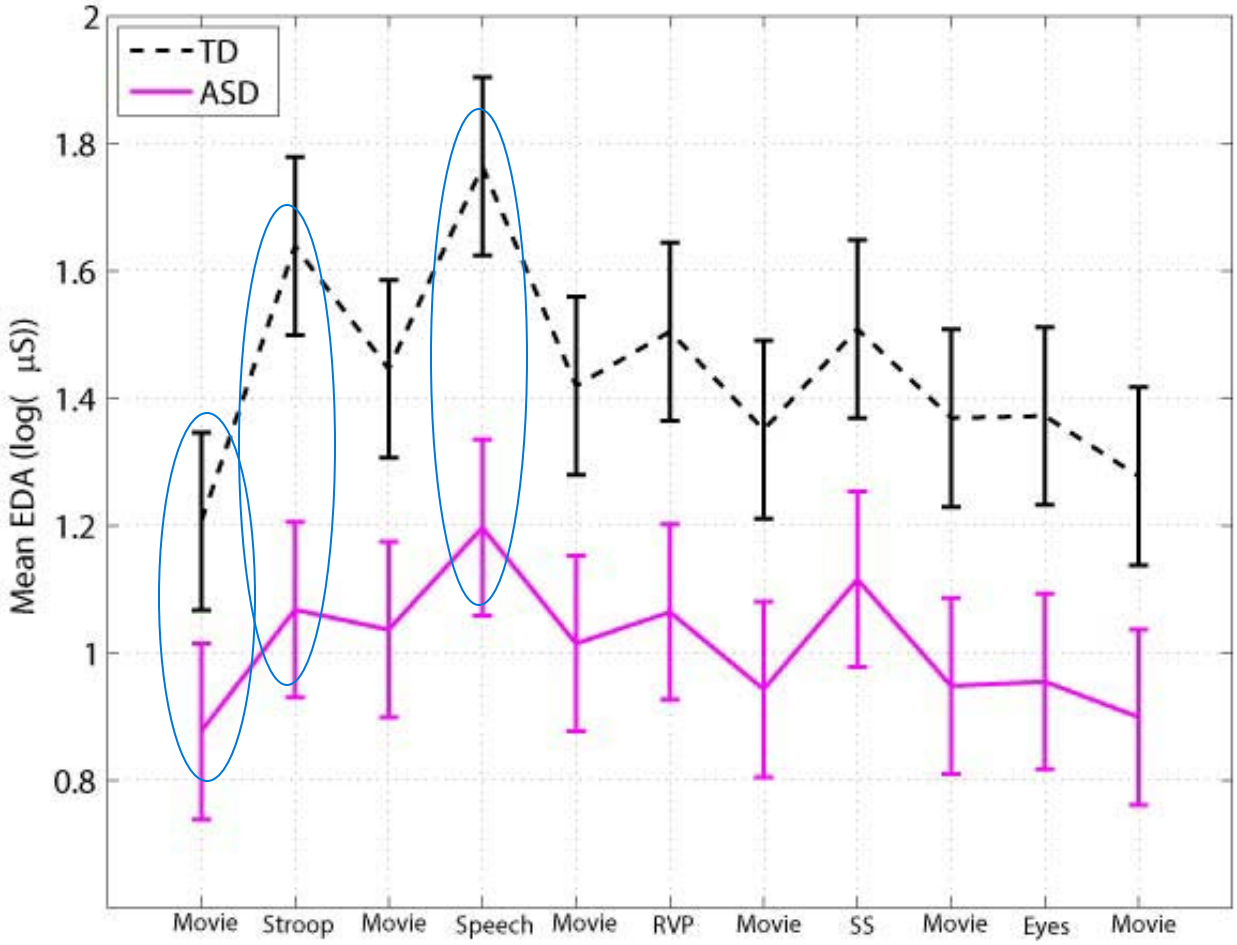
Results: Cardiac activity



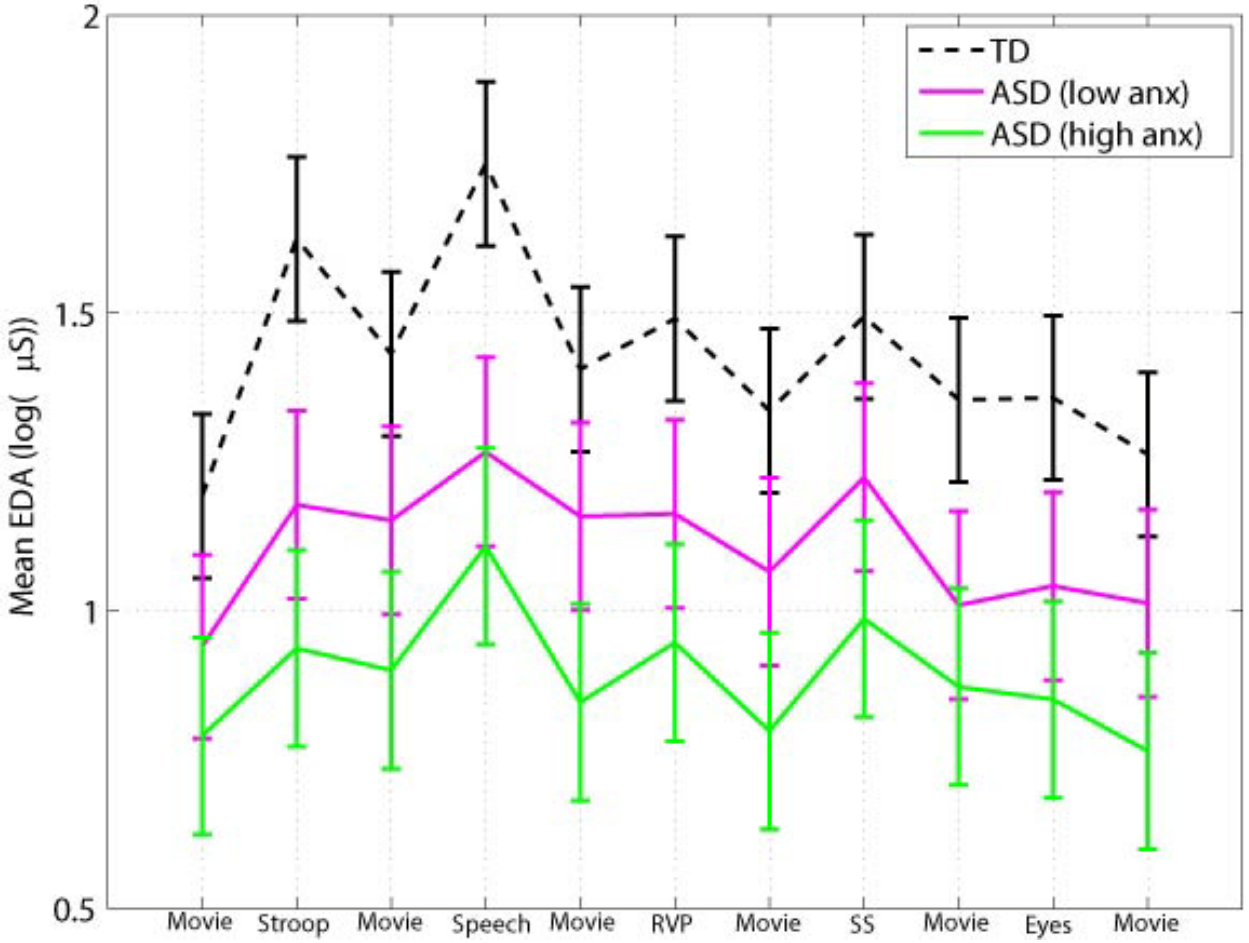


- Kushki et al 2014

Results: Electrodermal activity (EDA)



Results: Effect of anxiety



What does it mean of treatment development

- Construct confusion is a critical barrier to drug development
  - E.g. is anxiety in the general population the same biologic construct as in ASD
  - E.g. are the attention deficits seen in ADHD in the general population the same as those seen in children with ASD+ADHD
    - *If yes, treatments are available and treatment development in the general population is of relevance to ASD*
    - *If no, distinct drug development pathways needed to target the biological construct of such co-occurring conditions in ASD*
- How does lack of specificity of genomic findings for co-occurring neuropsychiatric conditions affect drug development

From disability to possibility