

ADHD AND DEFICIT IN SENSORIMOTOR GATING

Porfirio MC, Montanaro ML, Pennacchia S, Gennaro L, Vignati M, Curatolo P
 Unità Operativa di NPI, Clinica S. Alessandro, Università di Roma "Tor Vergata"



ChildNeurology T.M. Vignati P.T.V.
 Neuropsichiatria Infantile Università degli Studi di Roma Policlino Tor Vergata

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Reviews and Overviews

The Endophenotype Concept in Psychiatry: Etymology and Strategic Intentions

Irving I. Gottesman, Ph.D., Hon.
 F.R.C.Psych.

Todd D. Gould, M.D.

Endophenotypes, measurable components unseen by the unaided eye along the pathway between disease and distal genotype, have emerged as an important concept in the study of complex neuropsychiatric diseases. An endophenotype may be neurophysiological, biochemical, endocrinological, neuroanatomical, cognitive, or neuropsychological (including configured self-report data) in nature. Endophenotypes represent simpler clues to genetic underpinnings than the disease syndrome itself, promoting the view that psychiatric diagnoses can be decomposed or deconstructed, which can result in more straightforward—and successful—

genetic analysis. However, to be most useful, endophenotypes for psychiatric disorders must meet certain criteria, including association with a candidate gene or gene region, heritability that is inferred from relative risk for the disorder in relatives, and disease-association parameters. In addition to furthering genetic analysis, endophenotypes can clarify classification and diagnosis and foster the development of animal models. The authors discuss the etymology and strategy behind the use of endophenotypes in neuropsychiatric research and, more generally, in research on other diseases with complex genetics.

(Am J Psychiatry 2003; 160:636-645)

ADHD AND DEFICIT IN SENSORIMOTOR GATING

□ Current theoretical perspectives on ADHD focus on deficit of attention, inhibition or both

□ Despite important differences among these models, all acknowledge that ADHD likely involves poor inhibition

□ Neither attention nor inhibition has a single operational definition, and many tasks likely involve elements of both processes

□ Consequently, it has been suggested that investigators choose measures that most simply and directly assess the construct of interest (Douglas 1999; Sergeant et al., 1999)



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SENSORY MOTOR GATING ?

SCREENING (GATING-OUT OF AWARENESS) OF TRIVIAL STIMULI
 IN ORDER FOR SALIENT STIMULI TO BE PROPERLY PROCESSED

(Smith and Boyce, Psychopharmacology 2001)

PPI: DEFINITION

REDUCTION IN AMPLITUDE OF THE RESPONSE TO A STRONG
 STIMULUS, WHEN PRECEDED BY A RELATIVELY
 WEAK SENSORY EVENT (the prepulse stimulus)



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DEFICIT IN SENSORIMOTOR GATING IN ADHD

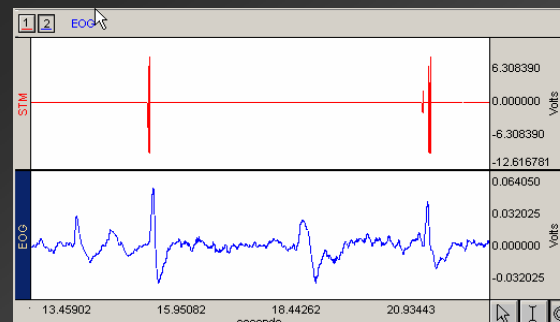
STARTLE RESPONSE: CONTRACTION OF FACIAL
 SKELETAL MUSCLES IN RESPONSE TO A STIMULUS



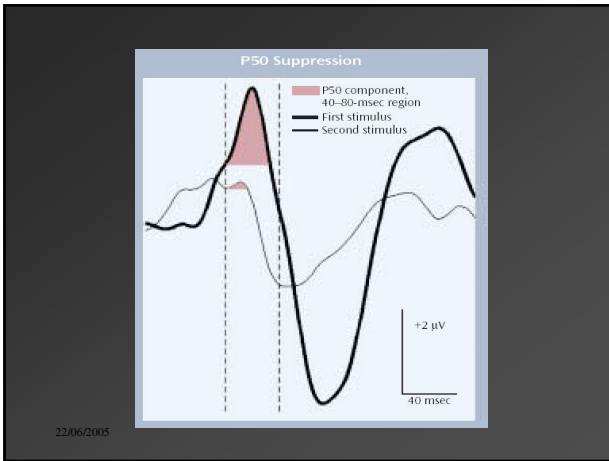
- DEFENSIVE RESPONSE
- TRANSLATIONAL
- PLASTICITY :
 - PPI/P50
 - HABITUATION
 - FEAR POTENTIATION

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Startle reflex modulation



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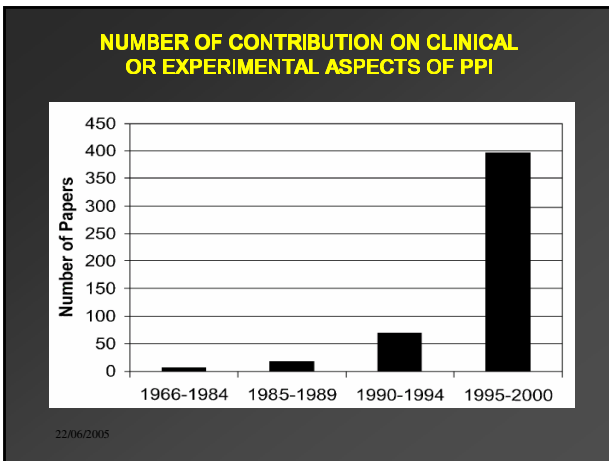
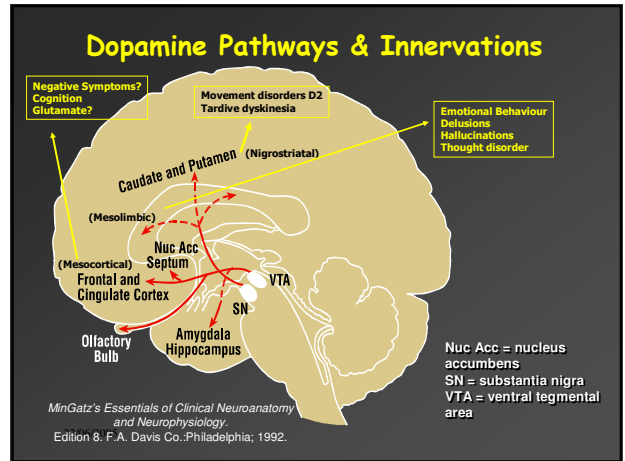
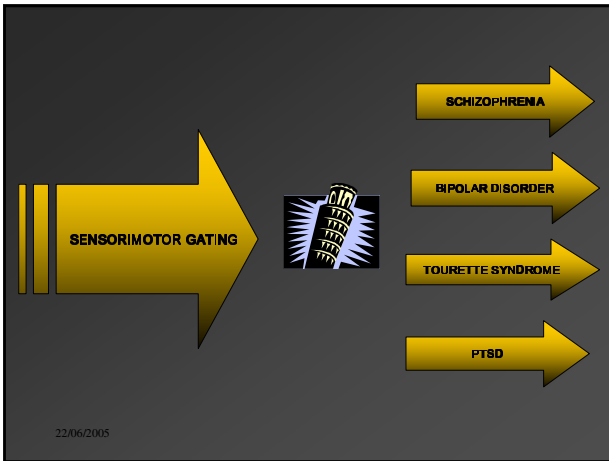
ENDOPHENOTYPE ?

- **Consistently abnormal in schizophrenic patients and in their clinically first degree relatives.**

Am J Psychiatry. 2000 Jan;157(1):55-9.
 "Sensory gating deficits assessed by the P50 event-related potential in subjects with schizotypal personality disorder".
Cadenhead KS, Light GA, Geyer MA, Braff DL.
 Department of Psychiatry, University of California, San Diego

- **Abnormal in patients with conditions linked to a deficit in *cortico-striato-pallido-pontine* circuit.**

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ENDOPHENOTYPE ?

➤ **Behav Brain Res. 2004 Oct 5;154(2):331-7.**

"Prepulse inhibition of acoustic startle in spontaneously hypertensive rats".
van den Buuse M.
 Behavioural Neuroscience Laboratory, Mental Health Research Institute (VI) Australia.

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ENDOPHENOTYPE ?

➤ **Biol Psychiatry. 2000 Jun 1;47(11):969-77.**

"The P50 auditory event-evoked potential in adult attention-deficit disorder: comparison with schizophrenia".

Olinic A, Ross RG, Harris JG, Young DA, McAndrews MA, Cawthra E, McRae KA, Sullivan B, Adler LE, Freedman R.
Department of Psychiatry, University of Colorado Health Sciences Center, Denver

➤ **Psychopharmacology (2003) 165:118-127**

"The effects of methylphenidate on prepulse inhibition during attended and ignored prestimuli among boys with attention-deficit hyperactivity disorder"

Hawk Jr. L.W., Yartz A. R., Pelham W. E., Lock T. M.
Department of Psychology and Psychiatry, State University of New York

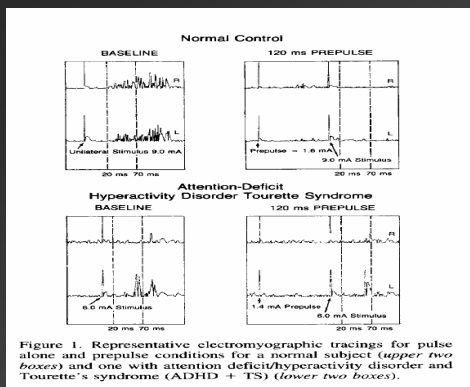
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Sensorimotor Gating in Boys with Tourette's Syndrome and ADHD: Preliminary Results

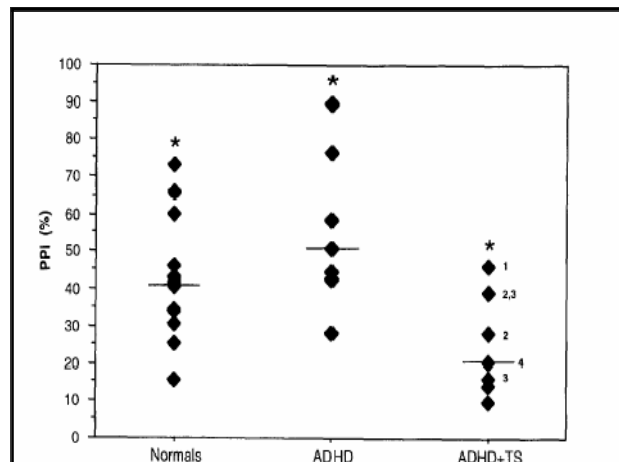
F. Xavier Castellanos, Edward J. Fine, Debra Kaysen, Wendy L. Marsh, Judith L. Rapoport, and Mark Hallett

BIOL PSYCHIATRY 1996;39:33-41

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MATERIAL AND METHODS

- 23 Children (21M/2F) with ADHD and internalizing disorders
- 23 Children with ADHD "alone"
- 25 Controls matched for age and sex
- All patients are aged 9 to 14 years and are diagnosed according to DSM-IV criteria for ADHD and received clinical questionnaires for ADHD and comorbid conditions
- All patients are drug free at moment of PPI study

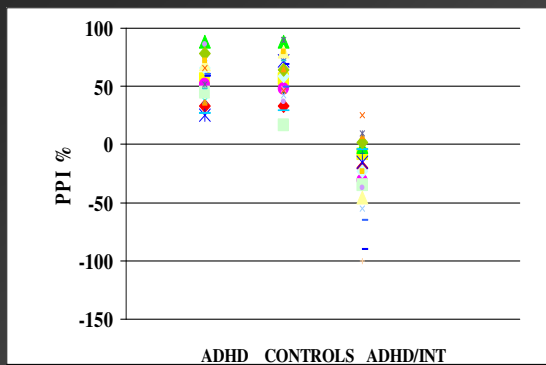
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MATERIAL AND METHODS

- Stimuli : broad-band (250 Hz – 50 KHz) square wave 1 msec duration 85 dB SPL
- Binaural presentation
- S1-S2 (SOA) intervals 500 msec
- Three blocks of twenty click pairs
- Intertrial interval: 8 sec

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RESULTS



DISCUSSION

Our patients did not differ significantly in the amplitude of pulse stimulus; differences in PPI can be ascribed to deficiencies in inhibition of the response in the presence of prepulse

Our data suggest that ADHD alone is not associated with a deficit in prepulse inhibition, which does not require any controlled attentional processing in the experimental stimuli

State's (due to hyperarousal) or trait's condition?

Correlation with dysfunction of amygdala circuit in this subgroup (with P50 deficit)?

fMRI studies of the amygdala regions are needed to understand neuroanatomical differences in these group of patients.

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Conclusions

- In summary, we consider these findings preliminary due to the limited size of our sample
- If independently replicated, these results might reflect a psychophysiological substrate in a subgroup of patients
- This correlation could also represent an important biological marker, increasing our understanding of the differences in responses to a pharmacological treatment and to monitoring clinical follow-up

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THANK YOU FOR ATTENTION



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