Individual Differences in Schizotypal Personality Traits and Dopamine Release

Neil D. Woodward, Ph.D.

Psychiatric Neuroimaging Program
Vanderbilt University School of Medicine

www.woodwardlab.com

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Schizotypal Personality Traits

• Schizotypal personality traits include:
  – Unusual perceptual experiences/odd beliefs
  – Paranoid ideation
  – Disorganized thoughts and behaviors
  – Excessive social anxiety and withdrawal

• Continuously distributed within general population
  – Isolated, odd beliefs=benign
  – Excessive levels associated with psychosocial dysfunction
    and Schizotypal Personality Disorder (SPD)

• ‘Normal’ variation in schizotypal traits associated
  with social adjustment and distress
Schizotypal Personality Traits and Schizophrenia Spectrum Disorders

- Variation in schizotypal traits organized into 3-4 factors:
  - Cognitive-perceptual/paranoid
  - Negative
  - Disorganized factors

- Pre-morbid personality in schizophrenia marked by an excess of schizotypal traits

- SPD is a risk factor for schizophrenia

- Covairates of schizotypal traits:
  - Deficits in sustained attention, working memory, sensory gating, and possibly eye movements
  - Low birth weight, low childhood SES, autumn/winter birth
Neural Correlates of Individual Differences in Schizotypy are Poorly Understood

- May relate to dopamine transmission

- Positron Emission Tomography (PET) imaging with dopamine receptor radioligands
  - Can be used to investigate dopamine function/dysfunction
  - PET imaging with displaceable ligands can be used to measure evoked dopamine release
    - Striatum: 11C-Raclopride, 123I-IBZM
    - Striatum + Extra-striatum: 18F-Fallypride

- PET studies in SPD and schizophrenia have revealed abnormalities in pre-synaptic dopamine function
Imaging Dopamine Release with PET

PRE-Synaptic

Baseline

POST-Synaptic

Amphetamine

Dö/D3 Receptor

Dopamine

Radio-labeled ligand

Binding Potential (BP)

↓BP
Imaging Dopamine Release with PET

PRE-Synaptic

Baseline

POST-Synaptic

Amphetamine

\[ \downarrow \text{BP} \]
Imaging Dopamine Release with PET

PRE-Synaptic

Amphetamine

POST-Synaptic

Baseline

\[ \text{D}_2/\text{D}_3 \text{ Receptor} \]

\[ \text{Dopamine} \]

\[ \text{Radio-labeled ligand} \]

Binding Potential (BP)

\( \downarrow \text{BP} \)
Striatal Dopamine Release is Elevated in Schizotypal Personality Disorder and Schizophrenia

Abi-Dargham et al. 2004; Laruelle et al. 1999
Striatal DA Release Correlates with Transient Increase in Positive Symptoms in Schizophrenia

- State component to increased dopamine release
- Not observed in SPD
  - Trait component?

Laurelle et al., 1999
Individual Differences in Schizotypy and Dopamine Release

• Evidence of an association between schizotypal traits and dopamine release would further support a trait basis for hyper-dopaminergia in schizophrenia

• Is dopamine release in extra-striatal brain regions related to schizotypy?
  • Indirect evidence in schizophrenia that extra-striatal dopamine function relevant to clinical symptoms
  • PET studies of dopamine release in SPD and schizophrenia have been restricted to striatum
Methods

• 49 Subjects (25 Men; Mean age=23.4±3.8)
  – No history of psychiatric disorder, substance abuse

• Subjects completed the Schizotypal Personality Questionnaire (SPQ) prior to scans

• Subjects scanned twice with 18F-fallypride
  – Baseline (34 subjects blind to drug administration)
  – 3.5 hrs after oral amphetamine (0.43 mg/kg)
D-Amphetamine Induced Dopamine Release Measured with 18F fallypride
Regions of Interest (ROIs)

- Whole Striatum
- Striatum functional sub-divisions:
  - Limbic/Ventral
  - Associative
  - Sensorimotor
- Additional ROIs
  - Thalamus
  - Hippocampus
  - Amygdala
Schizotypal Traits Correlate with Dopamine Release in the Striatum: ROI Results

* 1-tailed partial correlation after controlling for age, gender, and cohort

\[ r = 0.25, p < 0.05^* \]

\[ r = 0.29, p < 0.05^* \]
Schizotypal Traits Correlate with Dopamine Release in the Striatum: ROI Results

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* 1-tailed partial correlation after controlling for age, gender, and cohort
Schizotypal Traits Correlate with Dopamine Release in the Striatum: Voxel-wise* Results

* Corrected for whole striatum volume
Schizotypal Traits Correlate with Dopamine Release in the Striatum: Voxel-wise* Results

* Corrected for whole striatum volume
Schizotypal Traits Correlate with Dopamine Release in Extra-Striatal ROIs

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* 2-tailed Partial correlation after controlling for age, gender, and cohort
Extra-striatal Dopamine Release Correlates with Schizotypal traits: Voxel-wise* Results

* Whole brain corrected (p<.05 cluster level corrected)
## SPQ Factor Scores and Dopamine Release

### Schizotypal Personality Questionnaire Factor Scores

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<tr>
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Disorganized Schizotypal Traits Correlate with Dopamine Release in the Striatum: ROI Results

![Graphs showing correlation between SPQ: Disorganized Factor Score and Striatum DA Release](image)

- Left Striatum DA Release (R² Linear = 0.994)
- Right Striatum DA Release (R² Linear = 0.143)
Disorganized Schizotypal Traits Correlate with Dopamine Release: Voxel-wise* Results

* Whole Brain Corrected (p<.05 cluster level)
Disorganized Schizotypal Traits Correlate with Dopamine Release: Voxel-wise* Results

* Whole Brain Corrected (p<.05 cluster level)
Conclusions

• Amphetamine induced dopamine release correlates with individual differences in schizotypal traits

• Relationship observed in individuals with relatively low SPQ scores
  – Consistent with studies of cognition and sensory gating
  – Magnitude of correlation also consistent with other studies (r=.30 to .50)

• Association is independent of other personality characteristics including:
  – Extraversion
  – Novelty Seeking
  – Sensation Seeking
Limitations

• Modest levels of schizotypal traits
  – Replication in sample with higher level of schizotypy

• Lack of interview based measure of schizotypal traits
  – Sensitivity?

• State measures of psychotic-like symptoms
  – paranoia
Implications

• Further support for a trait component to hyper-dopaminergia in schizophrenia spectrum disorders

• Consistent with evidence of elevated pre-synaptic dopamine synthesis in:
  – Prodromal subjects
  – Unaffected siblings of schizophrenia patients
State and Trait Basis to Hyper-Dopaminergia

Data from Abi-Dargham et al., 2004 & Laruelle et al., 1999
Future Directions

• Implications for a psychosis continuum?

• Hyper-dopaminergia as an endophenotype of psychosis liability
  – Schizophrenia risk genes and dopamine release

• Cognitive disorganization and dopamine function
  – SPQ disorganized questions may be tapping subtle cognitive impairments
  – Frontal lobe function and striatal dopamine signaling

• Extra-striatal dopamine release in schizophrenia spectrum disorders