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Striatal Abnormalities and Spontaneous Dyskinesias in Non-Clinical Psychosis

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Abstract

Background—Accumulating evidence suggests that individuals experiencing non-clinical psychosis (NCP) represent a critical group for improving understanding of etiological factors underlying the broader psychosis continuum. Although a wealth of evidence supports widespread neural dysfunction in formal psychosis, there has been little empirical evidence to support our understanding of putative vulnerability markers or brain structure in NCP. In this study, we examined the neural correlates of spontaneous movement abnormalities, a neural biomarker previously detected in NCP that is linked to abnormalities in the striatal dopamine.

Methods—We screened a total of 1,285 adolescents/young adults, and those scoring in the upper 15 percentile on a NCP scale were invited to participate; 20 of those invited agreed and these individuals were matched with healthy controls. Participants were administered a structural scan, clinical interviews, and an instrumental motor assessment.

Results—The NCP group showed elevated force variability, smaller putamen (but not caudate), and there was a significant relationship between motor dysfunction and striatal abnormalities for the sample. Elevated force variability was associated with both higher positive and negative symptoms, and there was a strong trend ($p=.06$) to suggest that smaller left putamen volumes were associated with elevated positive symptoms.

Conclusions—The results are among the first to suggest an association between neural structure and a risk marker in NCP. Findings indicate that vulnerabilities seen in schizophrenia also characterize the lower end of the psychosis spectrum.

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Contributors

Dr. Mittal attained funding, conceptualized the study, conducted analyses, and drafted the manuscript. Drs. Orr and Turner helped to interpret data and to draft the manuscript. Mrs. Pelletier, Mr. Dean, Dr. Lunsford-Avery and Ms. Gupta helped to run the study, collect data, and draft the manuscript.

Conflict of Interest

There are no conflicts of interest to report.

Keywords

continuum; non-clinical psychosis; MRI; striatum; movement abnormality; spontaneous dyskinesia

I. Introduction

The developing research on non-clinical psychosis (NCP) holds considerable promise for clarifying understanding of the psychosis continuum (Ahmed et al., 2012; van Os et al., 2001). Further, a series of recent studies reports that this group of individuals (who experience one or more psychotic-like experiences in the absence of formal psychotic illness) is more likely to have comorbid disorders (e.g., anxiety, depression) (Armando et al., 2010; Nishida et al., 2010; Varghese et al., 2011), and also substantially heightened risk for psychotic disorders later in life (Hanssen et al., 2005; Poulton et al., 2000; Welham et al., 2009). These results suggest a critical need to understand vulnerability in this population. This is particularly noteworthy as the 5–8% median prevalence rate of NCP (van Os et al., 2009) reflects significant promise from a public health and early intervention perspective. Despite the necessity for a more thorough understanding, one critical area that is characterized by a dearth of empirical evidence relates to the biological characteristics of individuals reporting NCP (Kelleher and Cannon, 2011). As it stands, it is currently unclear if this group also exhibits vulnerability markers (e.g., structural/functional abnormalities) seen in formal psychotic disorders such as schizophrenia. This information is crucial for our emerging understanding of an important high-risk group, and from a broader perspective, stands to make considerable strides in elucidating the pathogenesis of psychosis.

Researchers argue that because NCP is not accompanied by significant 3rd variable confounds characteristic of schizophrenia (e.g., medications), understanding vulnerability markers in this group can substantially improve understanding of pathogenic processes. For example, a handful of related investigations have found that individuals with NCP show attenuated deficits (largely in-between what is observed in healthy control and formally psychotic groups) in a range of vulnerability characteristics seen in schizophrenia including cognitive deficits (Blanchard et al., 2010; Cannon et al., 2002; Horwood et al., 2008; Johns et al., 2004; Krabbendam et al., 2005), heritability/candidate genes (Foltynie et al., 2009; Lataster et al., 2009; Mittal et al., 2012c; Polanczyk et al., 2010), endocrine abnormalities (Mittal et al., 2013) and emotional processing (Pelletier et al., 2012). In addition, there have been few investigations of brain structure in this group, but the existing evidence does suggest abnormalities (Jacobson et al., 2010). Finally, a series of studies has suggested that NCP is associated with elevated subtle dyskinesias (Macmanus et al., 2012; Mittal et al., 2011a; Mittal et al., 2012c). However, there have been few studies designed to take the next step, and draw etiological conclusions about the relationships between these markers.

The study of motor abnormalities has a rich history for improving etiological understanding of psychosis, as investigations have shown that a failure to reach milestones, poor muscle development, and deficits in movement and coordination are among the first observable markers in premorbid populations (Fish, 1987; Walker, 1994). One key domain, spontaneous dyskinesias, describes the involuntary movements (e.g., jerking or flinging of the limbs, writhing of the fingers) that are independent of medication use (Puri et al., 1999) and believed to reflect the pathogenesis of psychotic disorders (Pappa and Dazzan, 2009). Spontaneous dyskinesias are the product of abnormal dopaminergic activity in the basal ganglia (DeLong and Wichmann, 2007). This has led to speculation that signs reflective of motor circuit dysfunction (i.e. striatal dopamine abnormalities) are potent risk markers, as they mirror dopaminergic abnormalities in an area that is also theorized to be critical in the

onset and maintenance of symptoms. Indeed, researchers have observed spontaneous dysketic movements in spectrum populations (Mittal and Walker, 2009; Mittal and Walker, 2011). Recently, we have extended this work by examining signs of subtle spontaneous dyskinesias in two distinct samples of NCP, and reporting abnormal movements when compared to low-NCP groups (Mittal et al., 2011a; Mittal et al., 2012c).

To date, there have been no studies of the underlying striatal structures in samples exhibiting NCP. In this investigation, we screened a large group of young adults ($n = 1,285$) and recruited a new sample exhibiting elevated NCP ($n=20$) for a structural imaging and movement assessment study. The aims were to 1) determine if striatal volumes were abnormal in NCP when compared to healthy controls ($n=20$), 2) replicate findings of elevated spontaneous dyskinesia in NCP, and 3) determine if these movement abnormalities were associated with a smaller striatal volumes (putamen and caudate) in the sample.

2. Methods

2.1 Participants

The recruitment strategy was designed to yield a high non-clinical psychosis (NCP) group and also a matched healthy control group representative of adolescents/young adults in the normal population. All participants in this Institutional Review Board (IRB) approved study were recruited through the Adolescent Development and Preventive Treatment (ADAPT) program. To identify participants for the non-clinical psychosis (NCP) group, the undergraduate research pool ($n=1,285$) was administered the Community Assessment of Psychic Experiences (CAPE) (Stefanis et al., 2002) positive symptom inventory. The option to participate in the study was made available to those scoring in the top 15th percentile on the CAPE positive domain (a score of 15 on the CAPE) that did not report any counter indications for scanning (e.g., metal in body, pregnancy). The research pool is a volunteer database in which undergraduate students taking an introduction to psychology course participate in research studies for course credit. Several studies recruit from this subject pool and to limit potential sampling bias (i.e., individuals knowingly selecting studies for which they are most interested in), available studies are listed as numbers without descriptions (study details were provided and informed consent was obtained upon arrival to ADAPT). From those eligible persons who were invited, a total of 20 elected to enroll (undergraduate volunteers choose randomly from a variety of studies they are invited to participate in), and upon arrival to ADAPT no one declined to participate after learning the details of the study. Although data was not available for the eligible individuals who did not select this study (those who enrolled in other studies instead did not consent for further assessment beyond the initial symptom and imaging eligibility screening), it is unlikely that there are any systematic differences with those who did participate as study selection was random. We broadened the inclusion from the 10th percentile mark used on our earlier study (Mittal et al., 2013) to capture a greater section of the psychosis continuum and allow for increased variability of NCP scores in the clinical group.

Healthy control participants ($n = 20$) were recruited through flyers and newspaper announcements (advertised as a study of neuroimaging and healthy development for volunteers with no family history of psychosis and no psychiatric symptoms) and selected on the basis of demographic characteristics comparable to the NCP group in age, sex, and parental educational level (a proxy for social class). The B module of Structured Clinical Interview for DSM-IV Disorders (SCID) (Overall and Gorham, 1976) was administered to participants in both groups to ensure that participants with elevated psychosis would not be included as this could potentially confound results (no participants were excluded based on this criterion). To maximize the potential to recruit a normative sample (and not an extreme low NCP group as we had in previous studies; (Mittal et al., 2012a; Mittal et al., 2012b;

Mittal et al., 2012c; Pelletier et al., 2012) screening with the CAPE positive domain was not an inclusion/exclusion criteria for the healthy control group.

2.2 Clinical Symptoms

The CAPE is self-report questionnaire that measures the frequency of psychotic-like experiences on a four-item Likert scale including “Never”, “Sometimes”, “Often”, and “Nearly Always” (Stefanis et al., 2002). The positive symptom section of the CAPE contains 20 items and is one of the most widely used, reliable, and well validated instruments for examining NCP (Barkus et al., 2007; Johns, 2005; Vellante et al., 2012). The negative symptom subscale of the CAPE (containing 14 items) was also administered to the sample. As noted, the B module of the SCID was used to identify psychotic disorders (an exclusion criterion), as formal psychosis could confound or drive findings. Previous studies show that the SCID yields valid and reliable diagnosis for a wide age range including young adults (Weinstein et al., 1999). This measure has been demonstrated to have excellent inter-rater reliability in adolescent populations (Martin et al., 2000). Advanced psychology doctoral students and clinical psychologists conducted the SCID interviews and reliability exceeded Kappa > .80.

2.3. Wide Range Achievement Test- Word Reading Subtest

A subsection of participants (UHR n=20, control n=14) were administered the Wide Range Achievement Test-Word Reading Subtest Fourth Edition (WRAT) as a measure of general intelligence. The WRAT is a well-validated and broadly used measure of achievement and broad learning ability for adolescents and young adults (Wilkinson & Robertson, 2006) and was used to determine if there were any group differences on general intelligence.

2.4 Measurement of dyskinesia using force variability

To detect subtle dyskinetic movements in the sample, we employed an instrumental measure that is capable of distinguishing the same subjects whose abnormalities are identified by standard observer-based severity ratings and also detecting an additional subset of the participants with sub-clinical movement abnormalities (i.e., roughly twice as many participants) (Cortese et al., 2005). Measurements of force instability involve having a subject use their dominant hand to apply and maintain a constant pressure on a load cell and maintain constant force over 20 seconds, while a computer program measures the amount of variability in the applied force (Mittal et al., 2011a). Specifically, participants are seated facing a monitor that displays the person’s force signal and a static target (equivalent to 350 cN of force). Participants are instructed to match a target with their signal (flexing index finger against transducer) and to maintain as steadily as possible until told to rest. Under normal circumstances the flexor digitorum profundus and the flexor digitorum superficialis (index finger flexor muscles) continuously and simultaneously contract to produce a near constant level of force against the load cell. However, in the presence of sub-clinical to clinical dyskinesia, these muscles contract with an irregular pattern, producing variable levels of force over a period of time (Cortese et al., 2005). The segment with the greater range in force (determined by computing the force minima and maxima over the medial 80% of each segment) is subjected to quantitative analysis of error that includes low pass filtering to remove any tremor. Final analysis of force error involved obtaining the coefficient of variation (CV) from the mean and standard deviation of the force waveform. The force variability (FV) measure has been validated as a measure of dyskinesia in studies of spontaneous dyskinesias (Cortese et al., 2005) and is highly reliable (Caligiuri et al., 1997).

2.5 Structural Imaging

Magnetic resonance imaging (MRI) of the brain was acquired on each subject using a Siemens 3-Tesla TIM Trio MRI scanner with 12-channel parallel imaging. A T1-weighted 3D magnetization prepared rapid gradient multi-echo sequence (MPRAGE; sagittal plane; repetition time [TR] = 2530 ms; echo times [TE] = 1.64 ms, 3.5 ms, 5.36 ms, 7.22 ms, 9.08 ms; GRAPPA parallel imaging factor of 2; 1 mm³ isomorphic voxels; FOV = 256mm; flip angle = 7°; 192 interleaved slices; time = 6:03 min) covering the whole brain was acquired for anatomic segmentation. A turbo spin echo proton density (PD)/ T2-weighted acquisition (TSE; axial oblique aligned with anterior commissure-posterior commissure line (AC-PC line); TR= 3720ms; TE=89ms; GRAPPA parallel imaging factor of 2; .9 × .9 mm voxels; FOV=240mm; flip angle: 120°; 77 interleaved 1.5mm slices; time = 5:14 min) was acquired to check for incidental pathology. The entire imaging protocol including localizing images, gradient echo field mapping, arterial spin labeling scan, and BOLD weighted resting state scan was about 30 minutes.

2.6 Image Processing

Target subcortical nuclei, including the putamen and caudate, were delineated automatically on the MPRAGE using the Freesurfer suite of automated tools (Fischl et al., 2002). The processing stream involved motion correction, removal of non-brain tissue using a hybrid watershed/surface deformation procedure (Segonne et al., 2004), automated Talairach transformation, segmentation of the subcortical white matter and deep gray matter volumetric structures (Fischl et al., 2002; Fischl et al., 2004) intensity normalization (Sled et al., 1998), tessellation of the gray matter white matter boundary, automated topology correction (Fischl et al., 2001; Segonne et al., 2007), and surface deformation following intensity gradients to optimally place the gray/white and gray/cerebrospinal fluid borders at the location where the greatest shift in intensity defines the transition to the other tissue class (Fischl and Dale, 2000). It should be noted that participant in the study were assessed for sub-clinical movements (very subtle movements) and it is not likely that any overt dyskinetic movements would have created an artifact (as noted, the B module of the SCID was administered to prevent inclusion of any participants with psychotic disorders, which are characteristic of more dramatic movement abnormalities such as hyperkinesias; Mittal & Walker, 2009). Freesurfer also calculates values for each participant's total intracranial volume (TICV) (i.e., the sum of whole-brain grey matter +white matter+cerebrospinal fluid), and each structure was divided by the TICV to control for whole brain volume.

2.7 Statistical Approach

Independent t-tests and chi-square tests were utilized to examine for any potential differences between the NCP and control groups in demographic characteristics. Likewise, group differences in the brain volumes, clinical variables, and force variability were examined using independent t-tests. Bivariate correlations were used to examine relationships between the symptoms, brain volumes, and force variability in the sample.

3. Results

There were no significant differences between NCP (n=20) and healthy control (n=20) groups on demographic characteristics including age, gender, general intelligence, and parental education. A Kolmogorov-Smirnov test revealed that the target variables met assumptions for parametric analyses. The NCP group showed a significantly higher total score on the positive domain when compared to the control group, $t(38)=8.01$, $p < 0.01$. Examples of the most endorsed items rated as "often or nearly always" include: "Do you ever feel as if electrical devices such as computers can influence the way you think?" (37.5%); "Do you ever feel that you are a very special or unusual person" (37.5%); "Do you

ever feel as if you are destined to be someone very important?" (35%); "Do you ever think that people can communicate telepathically?" (20%); "Do you believe in the power of witchcraft, voodoo, or the occult?" (15%); "Do you ever feel that people look at you oddly because of your appearance?" (10%); "Do you ever feel as if you are under the control of some force or power other than yourself?" (10%); and "Do you ever feel as if things in magazines or on TV were written especially for you?" (10%). The level of NCP positive symptoms endorsed is comparable to recent reports (Alemany et al., 2011). The NCP group also showed significantly elevated negative symptomatology when compared with healthy controls, $t(38)=3.76$, $p=.01$.

3.1 Force Variability

The NCP group exhibited significantly greater variability in force pressure when compared to the healthy controls, $t(38)=1.85$, $p=.05$. When compared with healthy controls, the NCP group showed smaller volumes for right, $t(42)=-2.90$, $p=.01$, and left putamen, $t(42)=-3.22$, $p=.01$ but differences for the right or left caudate did not approach significance (see Table 1).

3.2 Associations between force variability, striatal structures, and symptoms

Table 2 lists correlations between movement abnormality, symptom and striatal structure variables. There were significant negative associations between both the right and left putamen with force variability across the sample. These moderate correlations indicate that smaller putamen volumes were associated with greater levels of spontaneous movement abnormalities. It is also noteworthy that elevated force variability was moderately associated with more positive symptoms on the CAPE and moderate to strongly associated with more negative symptom frequency subscale. With regard to the structures, there was a trend level negative relationship between the left putamen and positive symptoms ($p=.06$) indicating smaller volumes were associated with elevated symptoms, but no associations between either symptom domain for bilateral caudate.

4. Discussion

There have been few structural imaging studies in NCP, and to our knowledge the present report represents the first empirical investigation to focus on striatal structures in this critical population. The observation that smaller putamen volumes are seen in the NCP group adds to our understanding of the psychosis spectrum, as striatal abnormalities are also characteristic of ultra high-risk groups and schizophrenia (Hokama et al., 1995; Mittal et al., 2010a; Taylor et al., 2005). Likewise, the finding of elevated spontaneous movement abnormalities in the clinical group are relevant, as they replicate previous investigations in NCP (Macmanus et al., 2012; Mittal et al., 2011a; Mittal et al., 2012c) and mirror a motor behavior observed in patients with schizophrenia (Fenton et al., 1997). Theoretical conceptions of schizophrenia have suggested that spontaneous dyskinesias are important as the same mechanism governing these movements may also drive and maintain psychosis (Mittal and Walker, 2009). Within this context, the present findings that the NCP group showed subtle spontaneous dyskinesias along with the association between smaller putamen volumes and the movement abnormalities suggest that a continuum of striatal vulnerability underlies the psychosis spectrum.

Hyperkinetic movements are commonly observed in patients receiving DA agonists (i.e., l-dopa, stimulants) and in diseases linked with altered striatal DA (e.g., Huntington's Chorea, Parkinson's disease, schizophrenia) (Cohen and Frank, 2009). Evidence also suggests that movement abnormalities manifest in a developmental trajectory that converges with changes posited by neurodevelopmental models of schizophrenia (Mittal and Walker, 2009;

Weinberger, 1987). These movements are of interest because they are more common in schizophrenia spectrum disorders (Boks et al., 2004) and occur in medication naïve populations (Pappa and Dazzan, 2009), suggesting they may, in part, reflect pathological processes underlying this spectrum of disorders. Spontaneous movement abnormalities have been observed in a range of premorbid, high-risk and spectrum samples. In a landmark study, Walker (1994) observed movement abnormalities including spontaneous dyskinesias in the early childhood videotapes of individuals who later developed schizophrenia as adults. Using a Danish high-risk cohort, researchers have also noted spontaneous dyskinetic movements in the high-risk offspring of patients with schizophrenia (Schiffman et al., 2004). Investigators have also noted these movement abnormalities in UHR groups as well (Mittal et al., 2007; Mittal et al., 2011b; Mittal et al., 2010b). While earlier efforts to study dyskinesias utilizing observer based interviews in the healthy relatives of schizophrenia patients did not detect differences, one recent study utilizing the more sensitive instrumentally based measures found elevated spontaneous movement abnormalities in the relatives of probands (Koning et al., 2011). To date, there are three independent investigations of spontaneous dyskinesias in NCP; one observing these movements in children utilizing an observer based coding method (Macmanus et al., 2012), and the other two utilizing an instrumentally based approach in adolescents and young adults (Mittal et al., 2011a; Mittal et al., 2012c). The present results support this body of literature, which taken together, speaks to a robust finding.

To date, the available structural imaging research focuses on cortical deficits in NCP. One important study examining 11–13 year-old children with subclinical psychotic symptoms found gray matter increases within the middle and superior temporal gyri, angular gyrus, orbitofrontal gyrus, and decreases in the inferior frontal gyrus (Jacobson et al., 2010). Recently, Cullen and colleagues (2012) utilized voxel-based morphometry (VBM) to examine youth aged 9–12 reporting antecedents of schizophrenia (including endorsed NCP items) and typically developing children (in the same sample reported in the Macmanus study described above; Macmanus et al., 2012). The investigators observed medial temporal lobe abnormalities including decreased gray matter volume in the right middle temporal gyrus, increased gray matter volume in the left superior-middle temporal gyri but this information was not examined in conjunction with movement variables (Cullen et al., 2012). Diffusion tensor imaging (DTI) studies have implicated white matter (WM) deficits in the inferior fronto-occipital fasciculus, cingulum and inferior longitudinal fasciculus (Jacobson et al., 2010). One interesting study found an increase in the magnetization transfer ratio (MTR) in the arcuate fasciculus (i.e., the major tract connecting frontal and temporal-parietal language areas) in schizophrenia and NCP participants but not in controls (de Weijer et al., 2011). A recent resting-state investigation observed increased connectivity between the left and right superior temporal regions and also between the left parahippocampal region and left inferior frontal gyrus (Dieren et al., 2012). Finally, functional studies have indicated reduced activity within the right frontal and bilateral temporal cortex for response inhibition and reduced activity in the anterior cingulate and middle frontal gyrus of error related processing (Jacobson et al., 2010). In a signal detection task (designed to illicit verbal hallucinatory phenomena under conditions of stimulus degradation), otherwise healthy individuals with high hallucination proneness reported a choice for signal to be present when it was not, and patterns of activation during these false alarms showed activation in the superior and middle temporal cortex (an area found to be active during hallucination in formal psychosis) (Barkus et al., 2007). Thus, while there is not a great deal of imaging research to inform our understanding, the available evidence supports the notion that those reporting NCP show dysfunction in structures and function also seen in patients with schizophrenia.

As noted, to our knowledge there are no studies aimed to determine subcortical structure in individuals exhibiting NCP. However, the present results mirror findings that smaller volumes for bilateral putamen, and not caudate, are associated with elevated spontaneous dyskinesias (on an observer based scale) in the psychosis prodrome (Mittal et al., 2010a). These results are also consistent with prominent theories relating to organization of the basal ganglia circuits, which suggest that motor functions pass through the putamen and cognitive functions and motivation are relegated to the caudate and ventral striatum respectively (Tekin and Cummings 2002). Given the elevated risk for schizophrenia seen in NCP in recent studies (Welham et al., 2009), it is noteworthy that UHR adolescents and young adults exhibiting spontaneous dyskinesias (Mittal and Walker, 2007; Mittal et al., 2010b) and smaller putamen (Mittal et al., 2010a) were more likely to convert to schizophrenia in a two-year period. The results are also consistent with findings of reduced putamen in schizophrenia (Dazzan et al., 2004). When examining NCP from a high-risk perspective, the present results are also noteworthy as an in vivo 18F-6-fluoro-L-dopa positron emission tomography (PET) observed that an elevated striatal DA uptake predates the onset of schizophrenia in UHR patients (Howes et al., 2009).

Present findings linking movement abnormalities to both positive and negative symptoms are quite intriguing. Frith (1987) first proposed that both the positive and negative symptoms of schizophrenia might be attributed to disturbances in volition (generation and monitoring of plans and actions), governed by frontostriatal function. Robbins (1990) argued that the heterogeneous range of core symptoms associated with psychosis, appearing to be associated with widespread structures and function, might be explained by an altered balance in the flow of information between cortico-striatal loops. Since then, researchers note that because the striatum is linked with forebrain structures involved in planning, goal-directed behavior, and monitoring intentions, irregular neuroactivation and/or compromised structural/neural circuitry could lead to a range of schizophrenia symptomatology (Graybiel, 1997).

Although the present study includes several improvements on our previous investigations of dyskinesias in individuals reporting NCPs (i.e., sampling for a healthy control group exhibiting a range of PLEs instead of an “extreme” low NCP group, including the B module of the SCID and employing a gold standard NCP assessment), there are some limitations as well. Our findings suggest a relationship between structural deficits and abnormal movements but do not show causality. Further, this present study focused on neural structure, but it is likely that spontaneous movement abnormalities reflect a more complex mechanism including connective tracts, receptors, and function. In a related point, the use of higher resolution structural imaging would allow for analysis of other highly relevant structures such as the subthalamic nucleus. Although there was not a significant difference in general intelligence between groups, there was a trend to suggest higher levels in healthy controls ($p=.15$) that would likely become significant with more statistical power. While this observation is generally consistent with a range of cognitive deficits reported in other NCP studies and research in youth at high-risk for psychosis (Walder et al., 2008; Siedman et al., 2010; Kelleher & Cannon 2011), the link between brain structure and intelligence is a noteworthy consideration (Wilke et al., 2003) and future studies with larger samples should aim to provide a more comprehensive intelligence battery in the entire sample and control for any group differences. Future investigations should screen for family history of psychosis, as this may be relevant to the phenotyping of subjects. In addition, it is important to note that the NCP construct is complex, and affected by numerous other interacting factors including environmental influences such as social disadvantage (Morgan et al., 2009) and cannabis use (Skinner et al., 2011). Future higher-powered studies should evaluate the affects of substance use, examine for any differences in those who experience distress related to the reported symptoms, and examine the middle percentiles on the CAPE.

Longitudinal imaging studies examining both connective (e.g., frontal subcortical circuits) and functional correlates theoretically associated with movement abnormalities will help to progress our understanding of NCP.

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Table 1**Participant Demographics, Symptoms, and Striatal Volume**

	Healthy Control	Non-Clinical Psychosis	Total	Group Differences
<u>Gender</u>				
Males	8(40.0%)	9(45.0%)	17(42.5%)	<i>N.S.</i>
Females	12(60.0%)	11(55.0%)	23(57.5%)	
Total	20	20	40	
<u>Age</u>				
Mean Years (SD)	18.4(1.6)	18.5(.8)	18.5(1.2)	<i>N.S.</i>
<u>Parent Education</u>				
Mean Years (SD)	15.2(3.2)	15.6(3.9)	15.4(3.5)	<i>N.S.</i>
<u>Wide Range Achievement Test</u>				
Mean (SD)	106.9(13.7)	100.4(11.8)	103.1(12.9)	<i>N.S.</i>
<u>CAPE Score</u>				
<i>Positive Symptoms</i>				
Mean (SD)	3.8(3.5)	18.6(7.4)	11.2(9.4)	<i>p</i> 0.01
<i>Negative symptoms</i>				
Mean (SD)	2.8(1.5)	5.1(2.2)	3.9(2.1)	<i>p</i> 0.01
<u>Force Variability</u>				
Coefficient of Variation (SD)	2.84(.91)	3.46(1.16)	3.15(1.07)	<i>p</i> 0.05
<u>Caudate</u>				
Right Mean % ICV (SD)	.25(.03)	.25(.03)	.25(.03)	<i>N.S.</i>
Left Mean % ICV (SD)	.25(.03)	.25(.03)	.25(.03)	<i>N.S.</i>
<u>Putamen</u>				
Right Mean % ICV (SD)	.38(.04)	.35(.03)	.37(.04)	<i>p</i> 0.01
Left Mean % ICV (SD)	.41(.04)	.37(.03)	.39(.04)	<i>p</i> 0.01

Note: not significant (N.S.); Non-clinical psychosis was derived from the positive symptom frequency subscale on the Community Assessment of Psychic Experiences (CAPE), which ranges from 0–60. The negative symptom subscale ranges from 0–42. Brain volumes represent the respective structure divided by total intracranial volume.

Table 2

Sample- Wide Associations Between Symptoms of Non-Clinical Psychosis, Striatal Volume, and Force Variability.

	Force Variability	Right Putamen	Left Putamen	Right Caudate	Left Caudate	Positive Symptoms	Negative Symptoms
<u>Force Variability</u>	--						
<u>Right Putamen</u>	-.31*	--					
<u>Left Putamen</u>	-.28*	.93**	--				
<u>Right Caudate</u>	-.09	.11	.25*	--			
<u>Left Caudate</u>	-.04	.15	.23	.90**	--		
<u>Positive symptoms</u>	.26*	-.14	-.25 [†]	.02	-.01	--	
<u>Negative symptoms</u>	.48**	-.02	-.09	-.15	-.08	.51**	--

**
p 0.01;

*
p 0.05;

[†]Trend level (p 0.10);

Sample- Wide associations include NCP and Control Groups; Positive and negative symptoms are from the Community Assessment of Psychiatric Experiences (CAPE).