Cognition and Brain Function in Schizotypy: A Selective Review

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Schizotypy refers to a set of personality traits thought to reflect the subclinical expression of the signs and symptoms of schizophrenia. Here, we review the cognitive and brain functional profile associated with high questionnaire scores in schizotypy. We discuss empirical evidence from the domains of perception, attention, memory, imagery and representation, language, and motor control. Perceptual deficits occur early and across various modalities. While the neural mechanisms underlying visual impairments may be linked to magnocellular dysfunction, further effects may be seen downstream in higher cognitive functions. Cognitive deficits are observed in inhibitory control, selective and sustained attention, incidental learning, and memory.

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In concordance with the cognitive nature of many of the aberrations of schizotypy, higher levels of schizotypy are associated with enhanced vividness and better performance on tasks of mental rotation. Language deficits seem most pronounced in higher-level processes. Finally, higher levels of schizotypy are associated with reduced performance on oculomotor tasks, resembling the impairments seen in schizophrenia. Some of these deficits are accompanied by reduced brain activation, akin to the pattern of hypoactivations in schizophrenia spectrum individuals. We conclude that schizotypy is a construct with apparent phenomenological overlap with schizophrenia and stable individual differences that covary with performance on a wide range of perceptual, cognitive, and motor tasks known to be impaired in schizophrenia. The importance of these findings lies not only in providing a fine-grained neurocognitive characterization of a personality constellation known to be associated with real-life impairments, but also in generating hypotheses concerning the aetiology of schizophrenia.

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Key words: schizophrenia/personality/perception/attention/memory/imagery/language/movement

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Introduction

Schizotypy refers to a constellation of personality traits thought to reflect the subclinical expression of schizophrenia in the general population.1,3 Schizotypy encompasses behaviors, cognitions, and emotions that resemble, at a less pronounced level of expression, the disturbances characteristic of schizophrenia. Psychometric self-report measures of schizotypy have been shown to yield 3 dimensions, viz. the positive, negative, and disorganized dimensions.2 Positive schizotypy describes perceptual aberrations akin to subsyndromal hallucinations as well as unusual ideas that resemble the delusions of schizophrenia. Negative schizotypy refers to a reduction in emotional, physical, and social functions such as the experience of pleasure or interest in social contacts. The disorganized dimension involves thought disorder as well as bizarre behavior.

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Although schizotypy is a risk factor for schizophrenia and schizophrenia-spectrum disorders,6,8 only a few people with high schizotypy scores become clinically ill, and there is considerable and stable interindividual variance in schizotypy across the entire spectrum from low to high scores. With schizotypy thus straddling the domains of personality psychology and psychiatry, we argue that the study of variation in schizotypy, even in samples with low-to-medium scores, is of importance for several reasons.

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First, the apparent phenomenological similarity of schizotypy with schizophrenia has implications for our understanding of the clinical condition. Specifically, schizophrenia is known not to be a binary phenotype (present/absent), suggesting the operation of multiple aetiological factors.8,7 Assuming that the resemblance between schizotypy and schizophrenia is not trivial,8 it is...
likely that at least partly overlapping aetiological factors underlie both phenotypes, making the study of similarities between the 2 an important contribution to aetiological research into schizophrenia. Additionally, an equally important but often neglected approach is the direct comparison of performance in people with high levels of schizotypy and patients with schizophrenia. Such work is critically needed to identify domains where schizotypy differs from schizophrenia, pointing to protective or compensatory mechanisms.

Second, people with high levels of schizotypy display maladaptive behaviors, such as smoking and drug use, and they suffer lower social, educational, and professional levels of functioning, impoverished quality of life, and high levels of distress (also see Cohen et al as well as Mohr and Claridge, this issue). Therefore, schizotypy is an important research topic in its own right because a characterization of cognitive and neural processes in schizotypy may improve our mechanistic understanding of these disturbances and aid the development of intervention strategies.

Indeed, the study of schizotypy is of importance to clinical and nonclinical research questions. A methodological advantage of this work is the absence of confounds that plague schizophrenia patient studies, such as long-term pharmacological treatment.

The additional and complementary consideration of schizotypal personality disorder (SPD) as well as genetic and clinical high-risk detection methods such as the identification of prodromal symptoms would also be of interest. However, for reasons of emphasis of this special issue, we focus on psychometrically identified schizotypy. When discussing studies on particularly high-scoring schizotypal individuals, we acknowledge that part of this population might also obtain a diagnosis of SPD. For example, Raine observed SPD in 5% of participants with schizotypal personality questionnaire (SPQ) scores in the top 10% of the distribution.

In the following sections, we provide a concise review of the pattern of performance in schizotypy in key domains of perception, cognition, and motor control. Wherever possible we discuss evidence of the neural correlates of these performance patterns. We particularly draw here on methods widely used in schizophrenia research, viz. electroencephalography (EEG) and functional magnetic resonance imaging (fMRI). Of course, this review is by no means exhaustive and we refer the reader to other reviews for further information. Following our review of these key findings we will discuss implications of this work for the study of schizophrenia.

**Cognition and Brain Function in Schizotypy**

**Perception**

At the core of schizotypy are unusual perceptual experiences across all sensory modalities (visual, auditory, olfactory, and somatosensory). Visual abnormalities in relation to schizotypy are already evident at early stages of processing, beginning with abnormal P1, backward-masking, localization, and depth perception. Schizotypy has also been associated with pervasive problems of perceptual organization.

The neural mechanism underlying visual impairments in schizotypy has been linked to magnocellular dysfunction. In addition, it has also been suggested to be linked to abnormal network coordination, especially synchronized oscillatory activity in schizotypy that measures the precision and degree to which neurons are recruited to a common network to perform specific visual and higher cognitive tasks. Interestingly, there are also associations of schizotypy with BOLD signal in perceptual networks during rest. A study of young individuals found positive correlations of SPQ positive, negative, and disorganized dimensions with functional connectivity in a visual network and negative correlations of the SPQ disorganized dimension with an auditory network. These findings suggest that functional connectivity in perceptual regions is related to schizotypy even in the absence of an active task, perhaps reflecting processes of imagery or social cognition.

Relatedly, it is important to note that “early” visual processing dysfunction may cascade to all stages of information processing with detrimental consequences. For example, abnormal P1, backward-masking, localization and so forth prevent high-fidelity encoding of stimulus and can lead to working memory (WM) problems. However, healthy individuals with elevated schizotypal traits are able to access compensatory mechanisms to achieve intact performance across a wide range of tasks.

Impaired early visual processing has been associated with overall elevated schizotypal traits, but also more specifically with the level of cognitive disorganization and with the positive syndrome. Sensory processing abnormalities are also consistently observed in the auditory domain. Auditory imprecision and reduced sensory gating are associated with increased schizotypy, parallel to the findings of auditory imprecision and abolished P50 in schizophrenia patients. However, auditory deficits in schizotypy tend to be subtle. For example, increased schizotypy is associated with reduced P3b and N2 amplitudes, but not with other event-related potentials such as N1, P2, and P3a. Similar to the case of visual abnormalities, early auditory impairments can lead to broader consequences.

There is also evidence of deficits in olfactory and somatosensory modalities, although these have not been as extensively examined, and olfactory deficits appear less clear than in visual or auditory perception. Elevated schizotypal traits have been associated with olfactory identification and detection but not with olfactory acuity. With respect to somatosensory and tactile functions, high schizotypy has been linked to higher 2-point
discrimination threshold, with implications for compromised parietal functioning.\textsuperscript{39}

Taken together, perceptual anomalies in relation to schizotypy are transmodal and persistent, with broad consequences for all aspects of behavior, as precise and efficient perceptual information processing lies at the heart of intact interaction with the external world.\textsuperscript{17}

Interestingly, despite evidence of early visual processing deficits, performance on a number of visuospatial tasks is essentially normal in high schizotypy,\textsuperscript{48} suggesting operation of compensatory strategies. These strategies can take the form of presenting the material for longer or the use of attention to enhance the temporal precision of the information processing\textsuperscript{41,42}; however, this needs testing in schizotypy.

In addition to early perceptual impairments, there is also an abundance of research showing impairments in higher cognitive processing in schizotypy, which we review in the next sections.

\subsection*{Attention and Memory}

Selective attention to a given stimulus involves both focusing awareness on the target and inhibiting internal representations of the competing distractor. Indeed, inhibitory failures have been identified as a core feature of schizophrenia since Bleuler.\textsuperscript{43} Individuals with schizophrenia and psychometrically identified individuals with high levels of schizotypy have also been shown to display sustained attention deficits. Individuals characterized by positive schizotypy\textsuperscript{44–47} and those characterized by negative schizotypy\textsuperscript{48} display poorer signal discriminability, as indexed by lower \(d'\) scores.

A more direct measure of inhibitory control is negative priming (NP). In a NP task, 2 stimuli are presented during the prime trial and the participant must focus on 1 and ignore the other. If on the subsequent trial, the previously ignored distractor is used as the new target, processing of the stimulus requiring the previously inhibited representation will be impaired, resulting in an increased reaction time; this is known as NP. Individuals with acute schizophrenia display reduced NP, indicating disinhibition.\textsuperscript{48–50} Importantly, it was shown that this deficit in schizophrenia is not due to methodological artefacts but instead represents a genuine inhibitory problem.\textsuperscript{48} With regards to schizotypy, elevated scores on the Perceptual Aberration scale\textsuperscript{51} were found to be associated with reduced NP on a spatial task.\textsuperscript{49} In another study,\textsuperscript{52} reduced NP on verbal tasks was observed in relation to higher scores on the Perceptual Aberration scale,\textsuperscript{51} Predisposition to Hallucinations scale,\textsuperscript{53} social anhedonia,\textsuperscript{54} and hypomania.\textsuperscript{55} Regression analyses in that study, however, showed that it was primarily a positive schizotypy factor that was related to NP\textsuperscript{52}.

An additional paradigm that has been widely used in schizophrenia and schizotypy research is latent inhibition (LI). In LI, exposure to an irrelevant stimulus prevents conditioning with the stimulus being formed at a later time. A well-replicated finding is that unmedicated schizophrenia patients with positive symptoms display reduced LI relative to healthy controls.\textsuperscript{56} Converging evidence based on investigations using verbal tasks,\textsuperscript{57} auditory tasks,\textsuperscript{58} and visual search tasks\textsuperscript{59} indicate that participants with higher scores on measures of positive schizotypy show a reduced LI effect.\textsuperscript{57,58,60}

Impairments in WM, the active storage, manipulation, and selection of responses to guide subsequent behavior, have emerged as one of the cardinal features of schizophrenia.\textsuperscript{61–63} Indeed, WM is considered a potential endophenotypic marker for the disorder. More subtle WM impairments have been reported in relation to elevated levels of positive\textsuperscript{64–66} as well as negative\textsuperscript{65,67,68} schizotypy. As mentioned earlier, WM deficits may reflect reduced down-stream accuracy of information processing that can already be indexed by early potentials.\textsuperscript{17,69} Furthermore, WM deficits in schizotypy may also explain some of the problems in daily functioning.

Other aspects of memory performance may also be adversely associated with elevated levels of self-reported schizotypal traits. In incidental learning, individuals are tested on the degree of the attention devoted to non-relevant stimuli by measuring how much of the nonattended material they recall. Regardless of the nature of the information assessed (ie, spatial or verbal), individuals with higher scores on measures of positive schizotypy had higher rates of incidental learning than individuals with lower schizotypy scores.\textsuperscript{70,71} In addition, participants with elevated levels of positive schizotypy show an absence of the expected enhancement of emotional memory.\textsuperscript{72} Finally, while LaPorte et al\textsuperscript{73} found no relationship between levels of positive schizotypy and verbal memory performance, Gooding and Braun\textsuperscript{74} observed an inverse relationship between negative schizotypy and nonverbal memory performance.

Research has also shown that attentional deficits as a function of (mainly positive) schizotypy might be biased in space, pointing to imbalances in hemispheric asymmetry with a potentially stronger right over left hemisphere activation.\textsuperscript{75} Individuals high in positive schizotypy show an attentional bias for small-scale (line bisection) and large-scale (spontaneous full-body navigation) spatial attention that is directed away from the right hemispace, reminiscent of the bias reported in patients with schizophrenia.\textsuperscript{76} Neuroimaging evidence for these aberrant laterality patterns have been published recently.\textsuperscript{76,77}

In summary, there is plenty of evidence showing that attention (selection and inhibition), WM and memory is reduced in schizotypy. There is evidence for both deficits in individuals with psychometrically identified schizotypy relative to individuals with low levels of schizotypal traits, as well as evidence for associations between specific deficits and specific schizotypal dimensions.
Imagery and Representation

Mental imagery may be construed as the process of active generation, inspection, and manipulation or transformation of internal representations. Mental imagery is also related to hallucinations but with a key difference in the perceived locus of agency. Enhanced subjective vividness of mental imagery has been reported in individuals with schizophrenia and elevated schizotypal traits in visual and auditory modalities. However, the link between vivid imagery experiences and hallucinations is weak or unclear.

In addition to vividness of mental imagery, some aspects of mental imagery manipulation appear enhanced in schizotypy. Mental rotation paradigms, which require mentally rotating a stimulus into a particular orientation relative to its own reference frame (allocentric mental rotation) or mentally rotating oneself into a particular orientation relative to the surrounding environment (egocentric mental rotation), allow for the parametric investigation of manipulation of internal representations. Both egocentric and allocentric mental rotation abilities have been investigated in relation to schizotypy. Faster allocentric mental rotation was associated with increased schizotypy and more specifically, negative schizotypy in women. Findings are mixed with respect to self-other transformation involving egocentric mental rotation. Both impaired, and enhanced egocentric mental rotation performance have been reported in relation to elevated schizotypy. These findings have implications for social cognitive abilities (see Cohen et al, this issue), notably theory-of-mind because one crucial aspect of mentalizing involves visuospatial perspective taking and simulation. Although enhanced egocentric perspective-taking ability may be associated with increased empathy, in particular in women, as a function of life experience, excessive perspective-taking could lead to reduced agency and dissociative experiences.

Language Production

Abnormalities of language are also seen in schizotypy, especially in higher-level language processing. Differences in production and interpretation of nonliteral language such as metaphors, irony, fauxpas, and proverbs, similar to schizophrenia and autism. While nonliteral language comprehension problems seem correlated with schizotypy across the spectrum, the association in nonclinical schizotypy is subtle but still detectable on the neural level. A number of mechanisms may contribute to these deficits, including semantic association differences, aberrant semantic priming mechanisms, and inadequate context integration.

Most likely both cerebral hemispheres contribute to language differences associated with elevated schizotypy, with the right hemisphere thought to play an important role in loosening of associations and pragmatic language deficits in schizotypy. Left fronto-temporal language network abnormalities may also explain language differences in schizotypy. Siever and Davis proposed that lateral temporal lobe deficits exist in both schizophrenia and SPD but are compensated by greater frontal capacity in schizotypy. This model is supported by a recent fMRI study in psychometric schizotypy. During comprehension of ironic remarks, healthy individuals with elevated schizotypy scores showed decreased bilateral temporal, but increased left prefrontal activation. A defective left hemisphere language system would also be compatible with the observation of N400 abnormalities and other functional neuroimaging evidence indicating reduced language lateralization. Yet, the consistency of such findings and their psychopharmacological mediation remain debated (see also Mohr and Claridge, this issue, on the link between language and creativity).

Motor Control

Individual differences in schizotypy have also been shown to be associated with alterations in the control of movements. Increased frequencies of neurological soft signs, considered to be endophenotypes of schizophrenia, have been reported in relation to schizotypy. Abnormalities in gait and reduced precision of manual motor control have also been found. Given the considerable knowledge base concerning motor control in the healthy brain, these findings can be used to gain insight into the neural alterations that underlie schizotypy. Specifically, neurological soft signs have in structural and functional neuroimaging studies been shown to tap a circuitry of cerebello-thalamo-prefrontal abnormalities.

Interestingly, studies of motor control may also have implications for our understanding of impairments in cognitive and social functioning in relation to schizotypy, given that movement perception and generation are often inextricably linked with communicative and cognitive processes. For example, a recent fMRI study observed that schizotypy is associated with neural alterations within the mirror neuron network during the imitation of actions: People with higher negative schizotypy scores showed decreased bilateral temporal, but increased left prefrontal activation. A defective left hemisphere language system would also be compatible with the observation of N400 abnormalities and other functional neuroimaging evidence indicating reduced language lateralization. Yet, the consistency of such findings and their psychopharmacological mediation remain debated (see also Mohr and Claridge, this issue, on the link between language and creativity).
understanding of brain functional changes in schizotypy and the role of clinically relevant personality traits in explaining inter-individual differences in such processes (for more detail on social processing in schizotypy, see Cohen et al, this issue).

In addition to manual motor control, a considerable body of evidence points to relatively subtle yet replicable impairments in oculomotor function in relation to high schizotypy. These studies originated in the observations of impairments in schizophrenia on a range of eye movement paradigms, including most prominently the smooth pursuit and antisaccade tasks. Extending this work, there is now considerable evidence of associations of higher schizotypy with impaired performance on smooth pursuit (following a slowly moving target) and antisaccades (making a rapid eye movement in the direction opposite to a sudden-onset peripheral target).

Pursuit deficits, which have been observed in both positive and negative schizotypy, involve a reduced ability to match eye velocity to target velocity. It has also been shown that the association between pursuit performance and schizotypy is observed particularly when pursuit eye movements are based on predictive processes, such as during target occlusion. Similar to deficits previously described in schizophrenia, a recent fMRI study provided first evidence for the neural alterations underlying the pursuit deficit in schizotypy. It was observed that individuals selected for high total scores of the O-LIFE short scale showed lower BOLD signal than controls with low O-LIFE scores in occipital areas that are known to be associated with early sensory and attentional processing as well as motion perception (V3A, middle occipital gyrus, and fusiform gyrus). This finding is compatible with evidence of motion processing deficits during smooth pursuit in schizophrenia patients.

Higher levels of both positive and negative schizotypy are also associated with an increased rate of direction errors on the antisaccade task. Recently, an fMRI study investigated the neural underpinnings of this deficit in relation to positive schizotypy. It was found that higher positive schizotypy scores were associated with reduced BOLD signal in posterior and subcortical areas such as putamen, thalamus, cerebellum, and visual cortex, similar to what is seen in patients with schizophrenia and their relatives. Interestingly, the reductions in activation in frontal areas that are also observed in some schizophrenia studies were not found. Neuroimaging evidence thus points to both shared networks of alteration in schizotypy and schizophrenia and differences.

Together these studies document subtle impairments in schizotypy, similar to the deficits in schizophrenia. Consideration of the neural level of explanation further extends the conclusions concerning overlap between schizophrenia and schizotypy: In neuroimaging studies, high schizotypy has been found to be associated with altered neural functioning, ie, reductions during antisaccades and pursuit and increases during motor imitation. Importantly, these studies also point to the sparing of some neural functions, such as the lack of frontal changes during antisaccades and pursuit that are observed in schizophrenia. While it must be cautioned that the latter data do not come from direct comparisons but rather from independent studies, it may be argued that the combined assessment of oculomotor and neural data allows the delineation of (neuro-cognitive) functions that may be spared in schizotypy, suggesting the operation of protective factors.

**Implications**

The reviewed literature paints a picture of relatively subtle yet widespread performance impairments in perceptual, cognitive, and motor functions, with notable exceptions of spared or improved functions such as imagery or allocentric mental rotation. A methodological strength of this work is the absence of secondary confounds that cloud experimental neurocognitive assessments in schizophrenia, such as pharmacological treatment or chronicity effects.

As mentioned earlier, a thorough description of the pattern of neurocognitive alterations in high schizotypy will help address with more confidence the question of the existence and nature of a possible continuum (or overlap) between schizotypy and schizophrenia. At the phenotypic level alone, this issue has not been resolved. Comparisons between high schizotypy and schizophrenia drawing upon neurocognitive data, however, may help resolve this question by yielding different possible scenarios. For example, are all the neurocognitive impairments of schizophrenia also seen in schizotypy, but at lower levels? Alternatively, are only some of the impairments of schizophrenia seen in schizotypy? A detailed examination of how the pattern of impairments in schizotypy compares to the impairments in schizophrenia will give us clues about the nature of the relationship between schizotypy and schizophrenia. Knowledge of these different kinds of patterns could significantly inform our understanding of the distribution of schizophrenia spectrum phenotypes across the population, without resorting to unspecified notions of a “continuum” between schizotypy and schizophrenia. Critically, direct comparisons across the entire spectrum, ie, low schizotypes, high schizotypes, and schizophrenia patients, are needed to address this question using the same tasks and paradigms. Research into the nature of the similarities and differences between schizophrenia and nonclinical schizotypy may also inform future development and validation of diagnoses for early clinical detection, such as the attenuated psychosis syndrome (APS).

Second, recent work suggests that the study of cognition and brain function in schizotypy may inform the development of experimental medicine model systems of...
schizophrenia with implications for drug development. The incomplete effectiveness of antipsychotic and pro-cognitive drugs represent an area of clear unmet need in schizophrenia and the development of new compounds is likely to benefit from model systems with well validated biomarkers."13,14 Applying the high schizotypy approach in an exploration of the validity of this model system it was recently shown that (1) WM impairments in high schizotypy were partly alleviated by amisulpride145 and (2) risperidone impaired antisaccade performance in medium schizotypal controls, whereas high schizotypals showed a numeric trend towards improvement.146 These recent data suggest that it may be possible to apply the schizotypy approach in drug development.

6.15 The methodological advantages of a schizotypy model system include the ready availability of participants that are recruited using relatively inexpensive, reliable and objective psychometric questionnaires. Importantly, schizotypy differs from other models of schizophrenia, such as ketamine or sleep deprivation, in that it may represent a better model of the neurodevelopmental aspects of schizophrenia, similar perhaps to the isolation rearing rodent model.147

6.25 Conclusions
In conclusion, this review has identified a number of perceptual, cognitive, and motor functions that deteriorate in relation to higher schizotypy. However, while there is generally consistent evidence of impairments in certain perceptual-motor abnormalities, there is considerable cross-study variability in higher cognitive deficits such as WM or top-down attentional control.40 Therefore, it is intriguing to speculate that compensatory mechanisms may be at play at higher levels of cognitive function. These may be detected as neurally inefficient activations in neuroimaging studies.48 It is also important to point out that the objective cognitive deficits described here may be relatively subtle and occur on the background of much more severe subjective cognitive complaints.40 Further research is needed, especially to identify not only domains of impairment in high compared with low schizotypy, but also to characterize areas of function that may be spared in high schizotypy compared to schizophrenia. Such work will not only further elucidate the cognitive processing pattern of individuals with high expressions of this personality constellation, but will also inform aetiological theories of schizophrenia.

6.50 References

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