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CRITICAL REVIEW

Cognitive and Prepulse Inhibition Deficits in Psychometrically High Schizotypal Subjects in the General Population: Relevance to Schizophrenia Research

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Abstract

Schizophrenia and schizotypal personality disorder share common clinical profiles, neurobiological and genetic substrates along with Prepulse Inhibition and cognitive deficits; among those, executive, attention, and memory dysfunctions are more consistent. Schizotypy is considered to be a non-specific ''psychosis-proneness,'' and understanding the relationship between schizotypal traits and cognitive function in the general population is a promising approach for endophenotypic research in schizophrenia spectrum disorders. In this review, findings for executive function, attention, memory, and Prepulse Inhibition impairments in psychometrically defined schizotypal subjects have been summarized and compared to schizophrenia patients and their unaffected first-degree relatives. Cognitive flexibility, sustained attention, working memory, and Prepulse Inhibition impairments were consistently reported in high schizotypal subjects in accordance to schizophrenia patients. Genetic studies assessing the effects of various candidate gene polymorphisms in schizotypal traits and cognitive function are promising, further supporting a polygenic mode of inheritance. The implications of the findings, methodological issues, and suggestions for future research are discussed. (*JINS*, 2012, *18*, 643–656)

Keywords: Schizotypy, Cognitive deficits, Prepulse inhibition, Endophenotypes, Schizotypal personality disorder, Neuropsychology, Early intervention

INTRODUCTION

Schizotypy usually is referred to as a "liability" to schizophrenia (Lenzenweger & Korfine, 1994), but it could also be referred to as non-specific "psychosis-proneness" (Claridge et al., 1996). There are two different perspectives on schizotypy: a psychological one with schizotypy representing deviant personality traits [i.e., individuals in the general population exhibit schizotypal traits on a continuum (Kendler et al., 1991) and psychosis represents extremes of normal variation in the healthy personality (Claridge, 1985; Eysenck & Eysenck, 1975)], and a psychiatric one with schizotypy representing attenuated psychotic symptoms (i.e., symptoms represent degrees of expression of the disease that are different from normal). The latter approach has given rise to the diagnostic criteria of Schizotypal Personality Disorder (SPD) (APA, 1980).

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Apart from the close relationship of SPD clinical characteristics to the clinical profile of schizophrenia, the two disorders also share common genetic (Siever & Davis, 2004), and neurobiological substrates (Dickey, McCarley, & Shenton, 2002; Siever & Davis, 2004) as well as cognitive impairments (Siever & Davis, 2004; Spaulding, Garbin, & Dras, 1989), which impact on patients' daily living (Green, 1996). Longitudinal studies also suggest that schizotypy may be a forerunner of schizophrenia (Chapman, Chapman, Kwapil, Eckblad, & Zinser, 1994). Accordingly, unaffected first degree relatives of schizophrenia patients present with high schizotypal traits (Laurent et al., 2001; Diwadkar, Montrose, Dworakowski, Sweeney, & Keshavan, 2006) and widespread cognitive impairments (Heydebrand, 2006; Hill, Harris, Herbener, Pavuluri, & Sweeney, 2008) and while the incidence of the illness in the general population is approximately 1%, adolescent offspring of schizophrenia patients are up to 15 times more likely to develop a psychotic disorder compared to the general population (Erlenmeyer-Kimling et al., 1995; Gottesman & Shields, 1982), with predicted conversion rates

approximating 40% (Diwadkar et al., 2006). Among the cognitive deficits observed in schizophrenia and SPD, impairments in executive functions, attention, and memory appear to be the most prevalent (Dickinson, Ramsey, & Gold, 2007; Fioravanti, Carlone, Vitale, Cinti, & Clare, 2005; Heinrichs & Zakzanis, 1998; Heydebrand, 2006; Laws, 1999; Matsui, Sumoyoshi, Kato, Yoneyama, & Kurachi, 2004; Matsui et al., 2007) and are, therefore, suggested as useful endophenotypes (Hill et al., 2008).

Schizophrenia and SPD have also been associated with deficits in information processing (Bleuler, 1911; Kraepelin, 1913). Prepulse Inhibition (PPI) of the startle reflex, a cross-species phenomenon, provides a valuable translational tool to study information processing abnormalities (Braff, 1993). PPI refers to a reduction in startle amplitude in response to a strong startling stimulus (pulse), if this is preceded shortly by a pre-stimulus (prepulse) too weak to elicit a measurable startle response itself. PPI is thought to reflect "sensorimotor gating," a form of central nervous system inhibition wherein irrelevant sensory information is filtered out during the early stages of processing so that attention can be focused on more salient features of the environment (Braff, Geyer, & Swerdlow, 2001). The sensory overload resulting from reduced sensorimotor gating is thought to give rise to cognitive fragmentation and some of the complex clinical symptoms associated with schizophrenia spectrum disorders (Braff, Grillon, & Geyer, 1992). It has been repeatedly demonstrated that patients with schizophrenia (Braff et al., 2001), their unaffected relatives (Thaker, 2008), and patients with SPD (Hazlett, Buchsbaum, Zhang et al., 2003, 2007, 2008) show deficient gating as measured by PPI. PPI is also considered a valid endophenotypic marker of psychosis (Braff & Light, 2005; Calkins et al., 2007).

Along with PPI, other neurophysiological endophenotypes, such as the P50 suppression and the P300 event-related potential, have undergone extensive review in the schizophrenia literature: schizophrenia patients and their unaffected relatives (for reviews, see Thaker, 2008; Turetsky et al., 2007), SPD patients (Cadenhead, Light, Geyer, & Braff, 2000; Mannan, Hiramatsu, Hokama, & Ohta, 2001; Trestman et al., 1996), and high schizotypal individuals in the general population (Arzy, Mohr, Michel, & Blanke, 2007; Evans, Gray, & Snowden, 2007; Sumich, Kumari, Gordon, Tunstall, & Brammer, 2008) present with deficits compared with normal controls. However, although the gating mechanisms accessed *via* PPI and these paradigms are often conceptually linked, there is evidence that they actually diverge in healthy and psychiatric populations (Brenner, Edwards, Carroll, Kieffaber, & Hetrick, 2004; Cadenhead, Light, Geyer, McDowell, & Braff, 2002; Light & Braff, 2001; Schwarzkopf, Lamberti, & Smith, 1993). Thus, these seemingly closely related gating abnormalities may be characteristic of different subgroups of patients, with PPI impairments being more specific to the gating deficits characteristic of schizotypy and unrelated to other deficient gating processes observed in schizotypal individuals (Cadenhead et al., 2002).

Apart from studying clinical populations or their biological relatives, another useful approach in endophenotypic research, is studying psychometrically defined schizotypal subjects in the general population [a review of general-population surveys indicated that schizophrenia-like experiences are observed in an attenuated form in 5–8% of healthy individuals (Van Os, Linscott, Myin-Germeys, Delespaul, & Krabbendam, 2009)]. This approach offers several advantages as it is devoid of several confounding variables such as medication and hospitalization effects, illness chronicity, psychosocial consequences of psychiatric diagnoses, and many others involved in the study of clinical populations (Gruzelier, 2003). It is worth noting that in accordance to schizophrenia (Bystritsky et al., 2001; Dworkin, Lewis, Cornblatt, & Erlenmeyer-Kimling, 1994; Harvey, 2011) and SPD patients (Dickey et al., 2005; Skodol et al., 2002), high schizotypal individuals in the general population also present with poor behavioral outcomes, such as reduced social functioning (Addington et al., 2011; Blanchard, Collins, Aghevli, Leung, & Cohen, 2011; Fonseca-Pedrero, Lemos-Giráldez, Paíno-Piñeiro, Villazón-García, & Muñiz, 2010; Henry, Bailey, & Rendell, 2008; Jahshan & Sergi, 2007; Seghers, McCleery, & Docherty, 2011), academic (Aguirre, Sergi, & Levy, 2008; Barrantes-Vidal, Lewandowski, & Kwapil, 2010) and occupational (Thaker, Adami, & Gold, 2001) difficulties, deteriorated socioeconomic status (Thaker et al., 2001), interpersonal problems (Aguirre et al., 2008; Barrantes-Vidal et al., 2010; Blanchard et al., 2011), and increased depressive and anxiety traits (Lewandowski et al., 2006; Seghers et al., 2011), resulting in poor quality of life (Cohen & Davis, 2009; Seghers et al., 2011). Also, from the standpoint of the psychological perspective described above, the study of schizotypal traits in the general population can yield findings that can be applied to clinical populations. As this perspective is proving to be a promising approach in the study of endophenotypes in schizophrenia spectrum disorders, studies of cognitive and PPI impairments in psychometrically high schizotypal subjects are increasing rapidly.

Schizotypy can be assessed either *via* interviews focusing on the detection of schizotypal traits [e.g., the Structured Interview for Schizotypy (Kendler, Lieberman, & Walsh, 1989)] or *via* self-report scales. The latter allows for several advantages compared with other forms of assessment as it is non-invasive, rapidly applied, easy to administer, score and interpret, and thus highly cost-effective. This psychometric strategy is also suggested to help identify individuals at risk that might not be detected by other approaches [e.g., the genetic high-risk paradigm (Gooding, Tallent, & Matts, 2007)]. Therefore, a variety of self-report assessment instruments have been developed [e.g., the Chapman Scales (Chapman, Chapman, & Raulin, 1976, 1978), the Schizotypal Traits Questionnaire (Claridge & Broks, 1984), the Schizotypal Personality Questionnaire (Raine, 1991), the Oxford-Liverpool Inventory of Feeling and Experiences (Mason, Claridge, & Jackson, 1995)] accompanied by adequate reliability and validity.

The aim of this critical review is to summarize findings on deficits in executive function, attention, memory, and PPI in psychometrically defined schizotypal, but otherwise healthy,

subjects and to contrast these with findings in schizophrenia patients and their unaffected first degree relatives. For this reason, a PubMed search was conducted with combinations of the general search terms "schizophrenia," "schizotypal," "schizotypy," "executive function," "attention," "memory," "prepulse inhibition," "genetic," and "healthy." A summary of the neuropsychological and PPI studies reviewed and their findings are presented in Tables 1 and 2, respectively.

EXECUTIVE FUNCTIONS' DEFICITS

Executive functions have long been synonymous with "frontal-lobe functions" but current definitions divide them into several interacting sub-processes (Miyake et al., 2000) mediated by a widely distributed brain network (Baddeley, Della Sala, Papagno, & Spinnler, 1997; Garavan, Ross, Li, & Stein, 2000). Therefore, "executive control," a broad term used to describe the neuropsychological processes incorporated in executive functions, refers to the interaction of a complex set of operations such as (a) initiation of behaviors and intentionality, (b) abstraction of patterns and concepts and giving meaning to stimuli based on prior experience, (c) prioritizing and assessing the emotional valence of stimuli, (d) holding information in working memory, (e) set shifting abilities and the ability to maintain set, (f) complex planning and problem solving, (g) response inhibition, and (h) strategy development, evaluation, and implementation (Frangou, 2010; Miller & Cummings, 2007).

Tasks that capture these different aspects of executive control have been developed, most of them being complex "multi-factorial" tasks (Stuss & Alexander, 2000, page 290) making it difficult to delineate these interweaving processes. The most widely used executive function tasks include the Wisconsin Card Sorting Test (WCST), the Stroop Color-Word test, the Controlled Oral Word Association test (COWAT), and the Trail Making test (TMT) (Strauss, Sherman, & Spreen, 2006). Adequate performance in these tasks requires the activation of cognitive processes other than executive functions [e.g., COWAT performance also relies on the integrity of information retrieval and recall (Henry & Crawford, 2005)]; however, they are still considered as executive function tasks, as successful performance requires efficient executive control (Palmer & Heaton, 2000). Meta-analytic studies in schizophrenia patients and their unaffected relatives indicate impaired performance in these tasks (Fioravanti et al., 2005; Heinrichs & Zakzanis, 1998; Henry & Crawford, 2005; Heydebrand, 2006; Stefanopoulou et al., 2009).

In studies examining schizotypy in the general population, high schizotypal subjects have been found to commit more total and perseverative errors, fail to maintain set and complete fewer categories (Gooding, Kwapil, & Tallent, 1999; Kim, Oh, Hong, & Choi, 2011; Lenzenweger & Korfine, 1994; Park, Holzman, & Lenzenweger, 1995; Suhr, 1997; Suhr & Spitznagel, 2001; Tallent & Gooding, 1999) in the WCST, with effect sizes ranging between medium (0.34) to high (0.86), although negative findings have also been reported (Hori et al., 2012; Noguchi, Hori, & Kunugi, 2008; Spitznagel & Suhr, 2002). The latter studies, however, are characterized by important methodological considerations, such as differences in sample characteristics compared with studies finding deficits (Hori et al., 2012; Noguchi et al., 2008), sampling biases and Axis II personality disorders not being examined at screening (Noguchi et al., 2008), limited number of participants and a lengthy assessment (Spitznagel & Suhr, 2002) or lack of corrections for multiple testing (Hori et al., 2012).

In studies using the COWAT, TMT, Stroop, Hayling, and Zoo Map tasks, no significant differences between low and high schizotypy groups were found (Kim et al., 2011; Laws, Patel, & Tyson, 2008; Suhr & Spitznagel, 2001; Spitznagel & Suhr, 2002). However, when further categorizing schizotypy into positive and negative, according to Crow's two syndrome concept of schizophrenia (Crow, 1985) [Type I: positive psychotic-like symptoms (e.g., magical ideation, ideas of reference, unusual perceptual experiences) generated by hyperdopaminergia in subcortical mesolimbic structures; Type II: negative symptoms (e.g., affective flattening, avolition, apathy, asociality) generated by hypodopaminergia in the prefrontal cortex], negative schizotypy was associated with poorer performance in the TMT (longer reaction times) and the Divergent Thinking task (fewer alternate uses) (Dinn, Harris, Aycicegi, Greene, & Andover, 2002). Also, in a study using cluster analysis that yielded three groups of schizotypal subjects (high negative dimension, high positive dimension, high on both dimensions), the cluster high on negative schizotypy performed worse on the WCST (Suhr & Spitznagel, 2001). The latter finding has been replicated and extended by Chang et al. (2011), who found that schizotypal subjects with high either negative or positive schizotypy completed fewer categories in the WCST compared with low negative or positive schizotypal individuals.

ATTENTION DEFICITS

Attentional impairments have long being recognized as one of the core characteristics of schizophrenia patients (Bleuler, 1911; Kraepelin, 1913) and are also reported in their unaffected first-degree relatives (Hill et al., 2008; Kéri & Janka, 2004). It has long been recognized that attention is a non-unitary construct. William James (1890) remarked that "Everyone knows what attention is. It is the taking possession by the mind, in clear and vivid form, of one out of what seem several simultaneously possible objects or trains of thought. Focalization, concentration of consciousness are of its essence. It implies withdrawal from some things in order to deal effectively with others, and is a condition which has a real opposite in the confused, dazed, scatterbrained state." Acknowledging that attention comprises several subprocesses, Coull (1998) in a comprehensive review based on insights from electrophysiology, functional neuroimaging, and psychopharmacology, categorized the different ways one can attend to stimuli as *attentional orientation* (direction of attention to a specific stimulus), *selective (or focused) attention* (attentional priority to a stimulus over another),

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Table 1. Neuropsychological impairments in psychometrically defined schizotypal subjects in the general population

Study	Sample characteristics N (F:M ratio); mean age (years) ± SD or age range	Task	Measures	Group differences/Correlations between SCT and cognitive measures	Statistical significance
Lenzenweger et al. (1991)	Con: N = 43 (21:22); 18.35 ± 0.53 SCT: N = 32 (20:12); 18.22 ± 0.55	CPT-Identical Pairs	Sensitivity index d' Hit rate	Con > SCT Con > SCT	$p < .05$ $p < .05$
LaPorte et al. (1994)	Low SCT: N = 30 High SCT: N = 20	Wechsler logical memory	Immediate and delayed recall; Retention rate	High SCT = Low SCT	$ps > .1$
Lenzenweger & Korfine (1994)	Con: N = 28 (13:15); 18.00 SCT: N = 23 (12:11); 18.00	WCST	Categories achieved Perseverative errors Failure to maintain set Trials to complete 1st category	Con > SCT Con = SCT Con < SCT Con < SCT	$p < .08$ $p > .1$ $p < .05$ $p < .09$
Park et al. (1995)	Low SCT: N = 23 (12:11); 18.96 ± 0.53 High SCT: N = 23 (14:9); 19.00 ± 0.52	WCST	Categories achieved Perseverative errors Failure to maintain set	Low SCT = high SCT Low SCT = high SCT Low SCT < high SCT	$p > .1$ $p > .1$ $p < .05$
		Delayed-response task[1]	Accuracy	Low SCT > high SCT	$p < .05$
Park & McTigue (1997)	Low SCT: N = 75; 19.1 years High SCT: N = 14; 19.1 years	Delayed-response task	Accuracy	Low SCT > high SCT	$p < .05$
Suhr (1997)	Con: N = 42 (24:18); 18.67 ± 0.65 SCT: N = 56 (31:25); 18.69 ± 0.74	WCST	Categories achieved Perseverative errors Failure to maintain set	Con = SCT Con < SCT Con = SCT	$p > .1$ $p < .005$ $p > .1$
		TMT	Part B	Con = SCT	$p > .1$
		COWAT	Correct responses	Con = SCT	$p > .1$
		Tower of Hanoi	Number of moves	Con = SCT	$p > .1$
		Stroop test	Interference score	Con>SCT	$p < .05$
Chen et al. (1998)	N = 345 (180:165); 41.3 ± 13.0	CPT	Hit rate (undegraded & degraded) False alarm rate (undegraded & degraded) Sensitivity index d' (undegraded & degraded)	Negative association with high SCT Negative association with high SCT Negative association with high SCT	$ps < .05$ $ps < .05$ $ps < .05$
Gooding et al. (1999)	Con: N = 104 (61:43); 18.72 ± 0.86 SCT: N = 155 (97:58); 18.73 ± 0.86	WCST	Categories achieved Perseverative errors Non-perseverative errors Failure to maintain set Trials to complete 1st category	Con > SCT Con < SCT Con = SCT Con < SCT Con = SCT	$p < .001$ $p < .001$ $p > .1$ $p < .05$ $p > .1$
Tallent & Gooding (1999)	Con: N = 63 (41:22); 19.11 ± 1.03 SCT: N = 115 (60:55); 18.94 ± 1.10	WCST	Categories achieved Failure to maintain set	Con > SCT Con < SCT	$p < .05$ $p < .05$
		Spatial working memory task[2]	Accuracy	Con > SCT	$p < .05$
Lenzenweger & Gold (2000)	Con: N = 26 (14:25); 18.96 ± 0.53 SCT: N = 31 (16:15); 19.00 ± 0.52	Word lists task[3] Letter-number span task[4]	Accuracy Accuracy	Con = SCT Con = SCT	$p > .1$ $p > .1$
Suhr & Spitznagel (2001)	Con: N = 49 (37:12); 18.00–19.00 years SCT: N = 59 (37:22); 18.00–19.00 years	WCST	Categories achieved Perseverative errors	Con > negative SCT Con < negative SCT	$p < .05$ $p < .005$
		TMT	Part B	Con = SCT	$p > .1$
		Stroop test	Interference score	Con = SCT	$p > .1$
Dinn et al. (2002)	Low SCT: N = 26 (17:9); 19.1 ± 1.3 median SCT: N = 60 (47:13); 18.9 ± 1.3 high SCT: N = 17 (11:6); 18.5 ± 0.9	TMT	Part A Part B	Low negative SCT <median = high Low negative SCT < median = high	$p < .05$ $p < .05$
		COWAT	Correct responses	NS differences	$p > .1$
		Divergent thinking task	Alternate uses	Low negative SCT > median = high	$p < .05$
		Stroop test	Interference score	NS differences	$p > .1$

(Continued)

Table 1. Continued

Study	Sample characteristics N (F:M ratio); mean age (years) ± SD or age range	Task	Measures	Group differences/Correlations between SCT and cognitive measures	Statistical significance
Spitznagel & Suhr (2002)	Con: N = 25 (19:6); 18.56 ± 0.72 SCT:N = 18 (10:8); 18.56 ± 0.71	WCST	Categories achieved	Con = SCT	$p > .1$
			Perseverative errors	Con = SCT	$p > .1$
			Failure to maintain set	Con = SCT	$p > .1$
		TMT	Part A	Con = SCT	$p > .1$
			Part B	Con = SCT	$p > .1$
		COWAT	Correct responses	Con = SCT	$p > .1$
		Stroop test	Interference score	Con = SCT	$p > .1$
Bergida & Lenzenweger (2006)	N = 305 (187:118); 30.05 ± 7.45	CPT-Identical Pairs	Errors	Positive association with high SCT	$p < .005$
			Sensitivity index d'	Negative association with high SCT	$p < .05$
Gooding et al. (2006)	Con: N = 137 (69:68); 19.04 ± 1.21 SCT: N = 256 (160:96); 18.80 ± 1.06	CPT-Identical Pairs	Sensitivity index d'	Con > SCT	$p < .05$
Cimino & Haywood (2008)	Low SCT: N = 18; 18.00–59.00 years High SCT: N = 18; 18.00–59.00 years	Stroop test	Speed accuracy	Low SCT < High SCT	$p < .05$
Kerns & Becker (2008)	Con: N = 34 (19:15); 18.80 ± 1.3 SCT: N = 32 (18:14); 18.50 ± 1.1	3-back task	Accuracy	Con > SCT	$p < .05$
Laws et al. (2008)	Low SCT: N = 32 (27:5); 19.97 years High SCT: N = 29 (24:5); 23.31 years	COWAT	Correct responses	High SCT = Low SCT	$p > .1$
		Zoo map	Time planning and time executing	High SCT = Low SCT	$ps > .1$
		Hayling sentence completion test	Response time automatic; Response time inhibition	High SCT = Low SCT	$ps > .1$
Matheson & Langdon (2008)	N = 100 (62:38); 18–50 years	Wechsler letter-number sequencing	Accuracy	Negative association with negative and positive SCT	$p < .05$
Le Pelley et al. (2010)	N = 115 (98:17); 20.1 ± 1.85	Learned irrelevance paradigm[4]	Compounds of relevant and irrelevant cues	Negative association with positive SCT	$p < .05$
Breeze et al. (2011)	Low SCT: N = 16 (11:5); 19.95 ± 4.3 High SCT: N = 18 (12:6); 21.53 ± 5.49	Selective attention task[5]	Switching reaction time	High SCT > Low SCT	$p < .05$
Chang et al. (2011)	Low SCT: N = 16 (8:8); 33.63 ± 8.55 High SCT: N = 15 (8:7); 36.73 ± 14.27	WCST	Categories achieved	High SCT > Low SCT	$p < .05$
			Perseverative errors	High SCT = Low SCT	$p > .1$
Hori et al. (2012)	N = 451 (339:112); 54.2 ± 15.2	WCST	Categories achieved	NS association	$p > .1$
			Perseverative errors	NS association	$p > .1$
			Total errors	NS association	$p > .1$
		Digit span	Accuracy	NS association	$p > .1$
Kim et al. (2011)	Con: N = 31 (31:0); 20.35 ± 1.60 SCT: N = 28 (28:0); 20.86 ± 2.14	WCST	Categories achieved	Con > SCT	$p < .05$
			Perseverative errors	Con < SCT	$p < .05$
			Total errors	Con < SCT	$p < .05$
		TMT	Part A	Con = SCT	$p > .1$
			Part B	Con = SCT	$p > .1$
		COWAT	Correct responses	Con = SCT	$p > .1$
		d2 test[6]	Errors	Con = SCT	$p > .1$
		CVLT	Short-term recall; Long-term recall; Recognition	Con = SCT	$ps > .1$

Con = Controls; F = Females; COWAT = Controlled Oral Word Association Test; CPT = Continuous Performance Test; CVLT = California Verbal Learning Task; M = Males; NS = Non-Significant differences; SCT = Schizotypy; TMT = Trail-Making Test; WCST = Wisconsin Card Sorting Test.

[1]For a description of the task see Park et al. (1995).
[2]For a description of the task see Tallent and Gooding (1999).
[3]For a description of the task see Lenzenweger & Gold (2000).
[4]For a description of the task see Le Pelley et al. (2010).
[5]For a description of the task see Breeze et al. (2011).
[6]For a description of the task see Kim et al. (2011).

Table 2. Prepulse Inhibition impairments in psychometrically defined schizotypal subjects in the general population

Study	Sample characteristics N (F:M ratio); mean age (years) ± SD or age range	PPI Paradigm	Group differences/Correlations between SCT and cognitive measures	Statistical significance
Simons & Giardina (1992)	Con: N = 20 (10:10) SCT: N = 18 (10:8)	Acoustic, un-instructed	Con > positive SCT	$p < .05$
Blumenthal & Creps (1994)	Con: N = 18 (10:8) SCT: N = 20 (10:10)	Acoustic, un-instructed	Con = SCT	$ps > .1$
Schell et al. (1995)	Con: N = 27 (16:11); 19.00 SCT: N = 42 (24:18); 19.00	Acoustic, instructed and un-instructed	Con > SCT in instructed paradigm compared to un-instructed	$p < .005$
Swerdlow et al. (1995)	Con: N = 20; 25.85 ± 1.92 SCT: N = 10; 24.8 ± 2.88	Acoustic, un-instructed	Con > SCT	$p < .05$
Cadenhead et al. (1996)	Con: N = 24 (14:10); 18.7 ± 1.1 SCT: N = 23 (13:10); 18.4 ± 0.8	Acoustic and tactile, un-instructed	Con = SCT	$ps > .05$
Abel et al. (2004)	N = 44 (17:27); 29.6 ± 4.0	Acoustic, un-instructed	No significant associations with PPI	$P > .05$
Evans et al. (2005)	N = 69 (57:12)	Acoustic, un-instructed	Negative association with high disorganisation factor of SCT	$p < .05$
Kumari et al. (2008)	N = 14 (0:14); 37.29 ± 11.48	Tactile, un-instructed	Negative association with high SCT	$p < .05$
Takahashi et al. (2010)	N = 79 (46:33); 38.5 ± 10.7	Acoustic, un-instructed	Negative association with high total, negative and positive SCT in females	$p = .005$; $p < .05$; $p = .005$

Con = Controls; F = Females; M = Males; PPI = Prepulse Inhibition; SCT = Schizotypy.

divided attention (alternating attention between more than two different stimuli), and *sustained attention* (attending to a stimulus for a long time).

Le Pelley, Schmidt-Hansen, Harris, Lunter, and Morris (2010) found deficient attentional allocation in high schizotypal subjects; sustained attention, as measured with Continuous Performance tasks, has also been consistently reported as deficient (Bergida & Lenzenweger, 2006; Chen, Hsiao, Hsiao, & Hwu, 1998; Chen, Hsiao, & Lin, 1997; Gooding, Matts, & Rollmann, 2006; Lenzenweger, Cornblatt, & Putnick, 1991). Selective attention impairments have been found (Breeze, Kirkham, & Mari-Beffa, 2011), although in one study using a Stroop test variation, selective attention was found to be intact in high schizotypal subjects, who, however, presented with lower switching capacity (Cimino & Haywood, 2008), bringing onto surface the interplay between attentional and executive control processes [e.g., resolving conflict among responses (Fan, McCandliss, Sommer, Raz, & Posner, 2002)].

MEMORY DEFICITS

Memory is another example of a cognitive process that can be further divided into several sub-processes. Thus, there is *declarative memory* (including episodic and semantic memory, memory for events and facts, respectively) and *non-declarative memory* (including procedural memory, non-associative learning, and classical conditioning) (Squire & Zola, 1996). Declarative memory impairments are consistently found in schizophrenia patients and their non-psychotic relatives (Aleman, Hijman, de Haan, & Kahn, 1999; Cirillo & Seidman, 2003; Dickinson et al., 2007; Fioravanti et al., 2005; Heinrichs & Zakzanis, 1998; Whyte, McIntosh, Johnstone, & Lawrie, 2005). Although non-declarative memory has not been extensively studied in schizophrenia, there is evidence suggesting that patients present with either mild (Altshuler et al., 2004) or no significant deficits (Goldberg, Saint-Cyr, & Weinberger, 1990; Schérer, Stip, Paquet, & Bédard, 2003) in procedural learning tasks. In healthy individuals, schizotypal traits are not consistently associated with either non-declarative (Ferraro & Okerlund, 1995) or declarative memory (Kim et al., 2011; LaPorte, Kirkpatrick, & Thaker, 1994; Lenzenweger & Gold, 2000).

Another categorization refers to the temporal characteristics of memory and distinguishes between *short-term (or working) memory* and *long-term memory*; working memory, also a component of executive function (Miller & Cummings, 2007), refers to temporary storage and manipulation of information while long-term memory refers to maintenance of information for longer time periods (Goldman-Rakic, 1994). Working memory impairments have been extensively reported in schizophrenia patients and their relatives (Aleman et al., 1999; Dickinson et al., 2007; Giakoumaki, Roussos, Pallis, & Bitsios, 2011; Hill et al., 2008; Lee & Park, 2005), in accordance with the prefrontal cortex hypoactivation characteristic of the disorder (Andreasen et al., 1997; Carter et al., 1998). Accordingly, studies in the general population indicate impaired working memory performance in indivi-

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duals reporting high schizotypal traits (Kerns & Becker, 2008; Matheson & Langdon, 2008; Park et al., 1995; Park & McTigue, 1997; Tallent & Gooding, 1999).

PREPULSE INHIBITION DEFICITS

Several studies have reported that patients with schizophrenia (for review, see Braff et al., 2001), even at first episode (Aggernaes et al., 2010; Hammer, Oranje, Fagerlund, Bro, & Glenthøj, 2011; Kumari, Fannon, Sumich, & Sharma, 2007; Ludewig, Geyer, & Vollenweider, 2003; Mackeprang, Kristiansen, & Glenthoj, 2002), have deficient PPI compared to controls; similarly, their unaffected relatives (for review see Thaker, 2008), and patients with SPD (Cadenhead, Geyer, & Braff, 1993; Cadenhead, Swerdlow, Shafer, Diaz, & Braff, 2000; Cadenhead et al., 2002; Hazlett, Buchsbaum, Zhang et al., 2003, 2007, 2008) also present with deficient PPI. PPI impairments have also been reported in high schizotypal subjects in the general population (Simons & Giardina, 1992; Swerdlow, Filion, Geyer, & Braff, 1995; Takahashi et al., 2010) accompanied by reduced activity in frontal, parietal and temporal brain regions (Kumari, Antonova, & Geyer, 2008). Smoking habits and attentional mechanisms have been suggested to modulate these effects, as significant negative associations between schizotypy and PPI were more notable in non-smoking subjects (Evans, Gray, & Snowden, 2005) and high-schizotypal subject failed to show the expected increase in PPI observed in instructed-PPI paradigms (Schell, Dawson, Hazlett, & Filion, 1995), when subjects are asked to attend to the stimuli.

Consistent with other research findings, negative results have also been reported (Abel, Jolley, Hemsley, & Geyer, 2004; Blumenthal & Creps, 1994; Cadenhead, Kumar, & Braff, 1996). The methodological limitations (e.g., small sample size, sample selection biases) of these studies are highlighted by the authors themselves making it more plausible that there is indeed an inverse relationship between schizotypal traits and PPI in the general population, as in schizophrenia and SPD.

GENETIC EFFECTS

As mentioned earlier, schizotypy is usually used to refer to the vulnerability intrinsic in all disorders included in the schizophrenia spectrum (Meehl, 1989). According to this view, schizotypes are those with a schizophrenia predisposing genotype who lack the effects of other modulatory factors (e.g., environmental stress) associated with manifest psychosis (Cannon, van Erp, & Glahn, 2002). Twin studies have shown SPD to be genetically related to schizophrenia (Kendler, Gruenberg, & Strauss, 1981; Kendler et al., 1993) and genetic influences with heritability ranging from 29% to 67% (Linney et al., 2003) have also been found in studies with twins from the general population. Genetic studies, however, indicate a polygenic mode of inheritance in schizophrenia (Karayiorgou & Gogos, 1997), making more plausible that only a subgroup of schizotypal subjects is genetically closer to schizophrenia patients (Faraone, Green, Seidman, & Tsuang, 2001). Even though this approach does not promise a comprehensive understanding of the disorder, early identification of the genetic architecture of this subgroup could have important early-intervention programme applications and therapeutic implications (Raine, 2006).

To this end, the gene encoding catechol-O-methyltransferase (COMT), an enzyme regulating dopamine activity in the prefrontal cortex (Badner & Gershon, 2002) contains the val158met functional single nucleotide polymorphism (SNP), which explains part of the inter-individual variance in executive function and working memory task performance (Bertolino et al., 2006; Egan et al., 2001) and predicts schizotypal personality characteristics (Avramopoulos et al., 2002; Schürhoff et al., 2007). In a study by Sheldrick et al. (2008), the COMT val158met genotype was associated in an allele dose-response manner to performance in the TMT test and the disorganization factor of schizotypy; the met/met (high dopamine) carriers performed better in the test and scored higher in the disorganization schizotypy scale, replicating the findings of Ma et al. (2007). However, an earlier study (Smyrnis et al., 2007) had found an opposite association, with the val/val (low dopamine) carriers scoring higher in disorganization and negative schizotypy dimensions, while no significant effects were found on cognitive performance.

Other candidate gene polymorphisms have also been examined, yielding conflicting results. Thus, the CGA carriers of the Proline Dehydrogenase (PRODH) gene haplotype that confers increased risk for schizophrenia (Li et al., 2004; Liu et al., 2002) presented with impaired PPI, verbal memory performance, and increased schizotypy (Roussos, Giakoumaki, & Bitsios, 2009). In another study by the same group (Roussos, Giakoumaki, Georgakopoulos, Robakis, & Bitsios, 2011) assessing the effects of the rs1006737 CACNA1C genetic variant, which has also been implicated in schizophrenia (Green et al., 2010), the risk allele was associated with increased schizotypal traits but no significant effects in cognitive task performance or PPI were found. Stefanis et al. (2007) found that none of four candidate genes (Neuregulin1 – NRG1; Dysbindin – DTNBP1; D-amino-acid oxidase activator – DAOA/G32 and D-amino-acid oxidase – DAAO) in schizophrenia pathology strongly modulated population variability in schizotypal features and cognitive functions. In a later study by the same group (Stefanis et al., 2008), the common T allele of the SNP rs951436 of the regulator of the G-protein signaling 4 (RGS4) gene was associated with negative schizotypy while there were no significant associations with cognitive endophenotypes. Genetic variation in another risk gene associated with increased risk for schizophrenia, the Zinc Finger Protein 804A (ZNF804A) (Yasuda et al., 2011) gene, has also been found to be associated with schizotypal features, while its effects on schizotypal features in relation to cognitive function have not yet been examined.

SUMMARY AND CONCLUSIONS

Understanding the relationship between schizotypal traits and cognitive function in the general population is a rapidly

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evolving field of research as it can significantly add to our understanding of schizophrenia. Executive function impairments are observed in high schizotypal subjects, in accordance with the schizophrenia literature; the most consistent findings seem to be with the WCST, a classical test of cognitive flexibility. Sustained attention Continuous Performance Tasks also provide consistent evidence for impaired performance in schizotypal subjects in analogy to schizophrenia. Regarding memory, the well-reported working memory deficits in schizophrenia are also found in high schizotypal subjects. Similarly, the PPI impairments observed in high schizotypal subjects suggest deficient sensorimotor gating, evident at the very early stages of the schizophrenia spectrum.

Studies in individuals from the general population (not stratified for schizotypy) have shown an association between PPI levels and performance on tasks assessing working memory, executive function and sustained attention (Bitsios & Giakoumaki, 2005; Bitsios, Giakoumaki, Theou, & Frangou, 2006; Csomor et al., 2008; Giakoumaki, Bitsios, & Frangou, 2006). PPI in humans is modulated by the prefrontal cortex (Hazlett, Buchsbaum, Zhang et al., 2008; Kumari et al., 2003, 2007), working memory, executive function, and attention are mediated by prefrontal activation (for reviews, see Chudasama, 2011; Kane & Engle, 2002; Wager & Smith, 2003) and high psychometric schizotypy is characterized by disturbed prefrontal function (Ettinger et al., 2011; Hori et al., 2008). While PPI is a pro-cognitive measure distinctly different from performance in tasks measuring neurocognition, these findings suggest either a causal relationship and/or overlapping brain circuitry, also involved in schizotypal processes.

The critical link between reduced PPI and cognitive deficits in high schizotypal subjects seems to be prefrontal dysfunction: in analogy to schizotypal traits, prefrontal dysfunction is lying on a dynamic continuum, the extreme position being occupied by schizophrenia, psychotic symptoms, pronounced PPI, and generalized cognitive deficits, followed by SPD, high schizotypy, and so on (Figure 1). This is supported by neuroimaging findings, indicating reduced gray matter volume in the prefrontal cortex of schizophrenia patients compared with controls, while SPD patients are intermediate (Hazlett, Buchsbaum, Haznedar et al., 2008; Matsui et al., 2008); accordingly, schizophrenia patients have been found to perform more poorly in sustained attention (Chan et al., 2009; Obiols et al., 1992), working memory (Cadenhead, Perry, Shafer, & Braff, 1999), and executive function (Cadenhead et al., 1999; Matsui et al., 2004) tasks and present with lower PPI (Hazlett et al., 2007) compared with high schizotypal individuals or SPD patients. As Kirrane and Siever (2000, page 62) suggested, "Better frontal 'buffering' (in SPD) may prevent the more severe cognitive and social deterioration associated with schizophrenia" and could also serve as a "protective" mechanism in high schizotypal individuals from the general population, preventing them from reaching the thresholds for a formal SPD diagnosis.

Genetic studies assessing the effects of various candidate gene polymorphisms in schizotypy, cognitive function, and PPI are limited and their findings are inconsistent. The

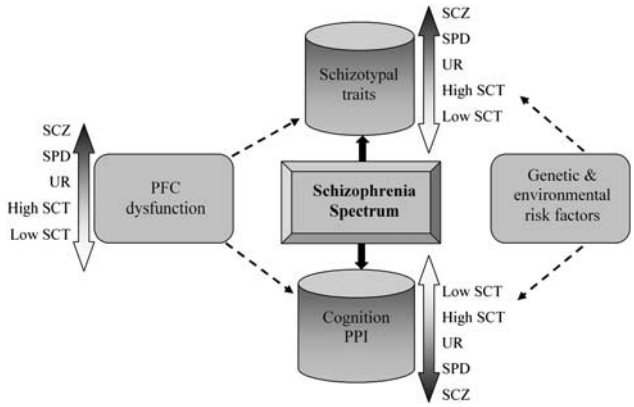

Fig. 1. Prefrontal dysfunction leads to schizotypal traits, cognitive and PPI deficits according to a continuum in the schizophrenia spectrum. Genetic and environmental risk effects act in concert and further modulate an individual's position in the continuum. PFC = Prefrontal; PPI = Prepulse Inhibition; SCT = Schizotypy; SCZ = Schizophrenia; SPD = Schizotypal Personality Disorder; UR = Unaffected Relatives.

effects of single genetic variants seem to be attenuated when examined separately, while their additive effects are more likely to exert significant influences on phenotypic measures, further supporting the polygenic mode of inheritance also observed in schizophrenia. Although inconclusive, these findings are very promising, when considering the extension and future application they can have in schizophrenia spectrum research.

Longitudinal studies in the general population have shown that individuals who report high schizotypal traits have an increased risk of transition toward schizophrenia-spectrum disorders (Chapman et al., 1994; Dominguez, Wichers, Lieb, Wittchen, & van Os, 2011; Gooding, Tallent, & Matts, 2005; Poulton et al., 2000; Welham et al., 2009). It is also well-established that as with schizophrenia, genetic and environmental influences act in concert and alter brain structure and function throughout development (Raine, 2006) in schizotypy (Figure 1). Although the effects of environmental influences have been studied extensively in schizophrenia (for review, see Brown, 2011), this is not the case with schizotypy. Thus, so far studies in high schizotypal individuals from the general population have focused on the effects of a limited number of environmental factors as risk indicators for the transition to psychosis, finding associations between high schizotypy and maternal exposure to influenza in pregnancy (Venables, 1996), physical or sexual abuse during childhood (Steel, Marzillier, Fearon, & Ruddle, 2009; Startup, 1999), migration (Linscott, Marie, Arnott, & Clarke, 2006), and season of birth (Cohen & Najolia, 2011; Hori et al., 2012). Therefore, based on the current findings we could hypothesize that the position one occupies in the schizophrenia spectrum is further modulated by the interaction of genetic and environmental risk factors.

Larger scale studies, including samples demographically and in general intellectual functioning closer to the patient samples reported in the literature, are needed to further

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elucidate similarities and/or differences in cognitive functions and sensorimotor gating between schizophrenia patients and high schizotypal subjects. Longitudinal studies should also examine the course of impairments in cognitive and sensorimotor gating functions as well as potential early and epigenetic effects and how they relate to the cognitive and PPI impairments and outcome of these individuals, as not all schizotypes convert into formally defined patients. This differential outcome pattern logically leads to another question. What kind of "advantage" protects a proportion of schizotypes from developing a psychotic disorder? Genetic, epigenetic, other personality factors, and most importantly their combined effects could serve as the underlying protective processes. Therefore, these protective factors are also very important to describe in future studies, as they can significantly aid not only the understanding of the etiopathogenesis of schizophrenia, but also the formulation and evaluation of intervention programs in schizophrenia-spectrum disorders.

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REFERENCES

Abel, K.M., Jolley, S., Hemsley, D.R., & Geyer, M.A. (2004). The influence of schizotypy traits on prepulse inhibition in young healthy controls. *Journal of Psychopharmacology*, *18*, 181–188.

Addington, J., Cornblatt, B.A., Cadenhead, K.S., Cannon, T.D., McGlashan, T.H., Perkins, D.O., … Heinssen, R. (2011). At clinical high risk for psychosis: Outcome for nonconverters. *American Journal of Psychiatry*, *168*, 800–805.

Aggernaes, B., Glenthoj, B.Y., Ebdrup, B.H., Rasmussen, H., Lublin, H., & Oranje, B. (2010). Sensorimotor gating and habituation in antipsychotic-naive, first-episode schizophrenia patients before and after 6 months' treatment with quetiapine. *International Journal of Neuropsychopharmacology*, *13*, 1383–1395.

Aguirre, F., Sergi, M.J., & Levy, C.A. (2008). Emotional intelligence and social functioning in persons with schizotypy. *Schizophrenia Research*, *104*, 255–264.

Aleman, A., Hijman, R., de Haan, E.H., & Kahn, R.S. (1999). Memory impairment in schizophrenia: A meta-analysis. *American Journal of Psychiatry*, *156*, 1358–1366.

Altshuler, L.L., Ventura, J., van Gorp, W.G., Green, M.F., Theberge, D.C., & Mintz, J. (2004). Neurocognitive function in clinically stable men with bipolar I disorder or schizophrenia and normal control subjects. *Biological Psychiatry*, *56*, 560–569.

American Psychiatric Association. (1980). *Diagnostic and statistical manual of mental disorders* (3rd ed.). Washington, DC: American Psychiatric Association.

Andreasen, N.C., O'Leary, D.S., Flaum, M., Nopoulos, P., Watkins, G.L., Boles Ponto, L.L., & Hichwa, R.D. (1997). Hypofrontality in schizophrenia: Distributed dysfunctional circuits in neuroleptic-naïve patients. *Lancet*, *349*, 1730–1734.

Arzy, S., Mohr, C., Michel, C.M., & Blanke, O. (2007). Duration and not strength of activation in temporo-parietal cortex positively correlates with schizotypy. *Neuroimage*, *35*, 326–333.

Avramopoulos, D., Stefanis, N.C., Hantoumi, I., Smyrnis, N., Evdokimidis, I., & Stefanis, C.N. (2002). Higher scores of self reported schizotypy in healthy young males carrying the COMT high activity allele. *Molecular Psychiatry*, *7*, 706–711.

Baddeley, A., Della Sala, S., Papagno, C., & Spinnler, H. (1997). Dual-task performance in dysexecutive and nondysexecutive patients with a frontal lesion. *Neuropsychology*, *11*, 187–194.

Badner, J.A., & Gershon, E.S. (2002). Meta-analysis of whole-genome linkage scans of bipolar disorder and schizophrenia. *Molecular Psychiatry*, *7*, 405–411.

Barrantes-Vidal, N., Lewandowski, K.E., & Kwapil, T.R. (2010). Psychopathology, social adjustment and personality correlates of schizotypy clusters in a large nonclinical sample. *Schizophrenia Research*, *122*, 219–225.

Bergida, H., & Lenzenweger, M.F. (2006). Schizotypy and sustained attention: Confirming evidence from an adult community sample. *Journal of Abnormal Psychology*, *115*, 545–551.

Bertolino, A., Caforio, G., Petruzzella, V., Latorre, V., Rubino, V., Dimalta, S., … Scarabino, T. (2006). Prefrontal dysfunction in schizophrenia controlling for COMT Val158Met genotype and working memory performance. *Psychiatry Research*, *147*, 221–226.

Bitsios, P., & Giakoumaki, S.G. (2005). Relationship of prepulse inhibition of the startle reflex to attentional and executive mechanisms in man. *International Journal of Psychophysiology*, *55*, 229–241.

Bitsios, P., Giakoumaki, S.G., Theou, K., & Frangou, S. (2006). Increased prepulse inhibition of the acoustic startle response is associated with better strategy formation and execution times in healthy males. *Neuropsychologia*, *44*, 2494–2499.

Blanchard, J.J., Collins, L.M., Aghevli, M., Leung, W.W., & Cohen, A.S. (2011). Social anhedonia and schizotypy in a community sample: The Maryland longitudinal study of schizotypy. *Schizophrenia Bulletin*, *37*, 587–602.

Bleuler, E. (1911). *Dementia praecox or the group of schizophrenias*. New York: International Universities Press.

Blumenthal, T.D., & Creps, C.L. (1994). Normal startle responding in psychosis-prone college students. *Personality and Individual Differences*, *17*, 345–355.

Braff, D.L. (1993). Information processing and attention dysfunctions in schizophrenia. *Schizophrenia Bulletin*, *19*, 233–259.

Braff, D.L., Geyer, M.A., & Swerdlow, N.R. (2001). Human studies of prepulse inhibition of startle: Normal subjects, patient groups, and pharmacological studies. *Psychopharmacology*, *156*, 234–258.

Braff, D.L., Grillon, C., & Geyer, M.A. (1992). Gating and habituation of the startle reflex in schizophrenic patients. *Archives of General Psychiatry*, *49*, 206–215.

Braff, D.L., & Light, G.A. (2005). The use of neurophysiological endophenotypes to understand the genetic basis of schizophrenia. *Dialogues in Clinical Neuroscience*, *7*, 25–135.

Breeze, J.M., Kirkham, A.J., & Mari-Beffa, P. (2011). Evidence of reduced selective attention in schizotypal personality disorder. *Journal of Clinical and Experimental Neuropsychology*, *33*, 776–784.

Brenner, C.A., Edwards, C.R., Carroll, C.A., Kieffaber, P.D., & Hetrick, W.P. (2004). P50 and acoustic startle gating are not related in healthy participants. *Psychophysiology*, *41*, 702–778.

Brown, A.S. (2011). The environment and susceptibility to schizophrenia. *Progress in Neurobiology*, *93*, 23–58.

Bystritsky, A., Liberman, R.P., Hwang, S., Wallace, C.J., Vapnik, T., Maindment, K., & Saxena, S. (2001). Social functioning and

quality of life comparisons between obsessive-compulsive and schizophrenic disorders. *Depression and Anxiety*, *14*, 214–218.

Cadenhead, K.S., Geyer, M.A., & Braff, D.L. (1993). Impaired startle prepulse inhibition and habituation in patients with schizotypal personality disorder. *American Journal of Psychiatry*, *150*, 1862–1867.

Cadenhead, K., Kumar, C., & Braff, D. (1996). Clinical and experimental characteristics of "hypothetically psychosis prone" college students. *Journal of Psychiatric Research*, *30*, 331–340.

Cadenhead, K.S., Light, G.A., Geyer, M.A., & Braff, D.L. (2000). Sensory gating deficits assessed by the P50 event-related potential in subjects with schizotypal personality disorder. *American Journal of Psychiatry*, *157*, 55–59.

Cadenhead, K.S., Light, G.A., Geyer, M.A., McDowell, J.E., & Braff, D.L. (2002). Neurobiological measures of schizotypal personality disorder: Defining an inhibitory endophenotype? *American Journal of Psychiatry*, *159*, 869–871.

Cadenhead, K.S., Perry, W., Shafer, K., & Braff, D.L. (1999). Cognitive functions in schizotypal personality disorder. *Schizophrenia Research*, *37*, 123–132.

Cadenhead, K.S., Swerdlow, N.R., Shafer, K.M., Diaz, M., & Braff, D.L. (2000). Modulation of the startle response and startle laterality in relatives of schizophrenic patients and in subjects with schizotypal personality disorder: Evidence of inhibitory deficits. *American Journal of Psychiatry*, *157*, 1660–1668.

Calkins, M.E., Dobie, D.J., Cadenhead, K.S., Olincy, A., Freedman, R., Green, M.F., … Braff, D.L. (2007). The Consortium on the Genetics of Endophenotypes in Schizophrenia: Model recruitment, assessment, and endophenotyping methods for a multisite collaboration. *Schizophrenia Bulletin*, *33*, 33–48 .

Cannon, T.D., van Erp, T.G., & Glahn, D.C. (2002). Elucidating continuities and discontinuities between schizotypy and schizophrenia in the nervous system. *Schizophrenia Research*, *54*, 151–156.

Carter, C.S., Perlstein, W., Ganguli, R., Brar, J., Mintun, M., & Cohen, J.D. (1998). Functional hypofrontality and working memory dysfunction in schizophrenia. *American Journal of Psychiatry*, *155*, 1285–1287.

Chan, R.C., Wang, Y., Cheung, E.F., Cui, J., Deng, Y., Yuan, Y., … Gong, Q. (2009). Sustained attention deficit along the psychosis proneness continuum: A study on the Sustained Attention to Response Task (SART). *Cognitive and Behavioral Neurology*, *22*, 180–185.

Chang, T.G., Lee, I.H., Chang, C.C., Yang, Y.K., Huang, S.S., Chen, K.C., … Chang, Y.H. (2011). Poorer Wisconsin card-sorting test performance in healthy adults with higher positive and negative schizotypal traits. *Psychiatry and Clinical Neurosciences*, *65*, 596–599.

Chapman, J.P., Chapman, L.J., & Raulin, M.L. (1976). Scales for physical and social anhedonia. *Journal of Abnormal Psychology*, *85*, 374–382.

Chapman, L.J., Chapman, J.P., Kwapil, T.R., Eckblad, M., & Zinser, M.C. (1994). Putatively psychosis-prone subjects 10 years later. *Journal of Abnormal Psychology*, *103*, 171–183.

Chapman, L.J., Chapman, J.P., & Raulin, M.L. (1978). Body-image aberration in schizophrenia. *Journal of Abnormal Psychology*, *87*, 399–407.

Chen, W.J., Hsiao, C.K., Hsiao, L.L., & Hwu, H.G. (1998). Performance of the Continuous Performance Test among community samples. *Schizophrenia Bulletin*, *24*, 163–174.

Chen, W.J., Hsiao, C.K., & Lin, C.C. (1997). Schizotypy in community samples: The three-factor structure and correlation with sustained attention. *Journal of Abnormal Psychology*, *106*, 649–654.

Chudasama, Y. (2011). Animal models of prefrontal-executive function. *Behavioral Neuroscience*, *125*, 327–343.

Cimino, M., & Haywood, M. (2008). Inhibition and facilitation in schizotypy. *Journal of Clinical and Experimental Neuropsychology*, *30*, 187–198.

Cirillo, M.A., & Seidman, L.J. (2003). Verbal declarative memory dysfunction in schizophrenia: From clinical assessment to genetics and brain mechanisms. *Neuropsychology Review*, *13*, 43–77.

Claridge, G. (1985). *Origins of mental illness*. Oxford: Blackwell Publishing.

Claridge, G., & Broks, P. (1984). Schizotypy and hemisphere function: I. Theoretical considerations and the measurement of schizotypy. *Personality and Individual Differences*, *5*, 633–648.

Claridge, G., McCreery, C., Mason, O., Bentall, R., Boyle, G., Slade, P., & Popplewell, D. (1996). The factor structure of "schizotypal" traits: A large replication study. *British Journal of Clinical Psychology*, *35*, 103–115.

Cohen, A.S., & Davis, T.E. (2009). Quality of life across the schizotypy spectrum: Findings from a large nonclinical adult sample. *Comprehensive Psychiatry*, *50*, 408–414.

Cohen, A.S., & Najolia, G.M. (2011). Birth characteristics and schizotypy: Evidence of a potential "second hit". *Journal of Psychiatric Research*, *45*, 955–961.

Coull, J.T. (1998). Neural correlates of attention and arousal: Insights from electrophysiology, functional neuroimaging and psychopharmacology. *Progress in Neurobiology*, *55*, 343–361.

Crow, T.J. (1985). The two-syndrome concept: Origins and current status. *Schizophrenia Bulletin*, *11*, 471–486.

Csomor, P.A., Stadler, R.R., Feldon, J., Yee, B.K., Geyer, M.A., & Vollenweider, F.X. (2008). Haloperidol differentially modulates prepulse inhibition and p50 suppression in healthy humans stratified for low and high gating levels. *Neuropsychopharmacology*, *33*, 497–512.

Dickinson, D., Ramsey, M.E., & Gold, J.M. (2007). Overlooking the obvious: A meta-analytic comparison of digit symbol coding tasks and other cognitive measures in schizophrenia. *Archives of General Psychiatry*, *64*, 532–542.

Dickey, C.C., McCarley, R.W., Niznikiewicz, M.A., Voglmaier, M.M., Seidman, L.J., Kim, S., & Shenton, M.E. (2005). Clinical, cognitive, and social characteristics of a sample of neuroleptic-naive persons with schizotypal personality disorder. *Schizophrenia Research*, *78*, 297–308.

Dickey, C.C., McCarley, R.W., & Shenton, M.E. (2002). The brain in schizotypal personality disorder: A review of structural MRI and CT findings. *Harvard Review of Psychiatry*, *10*, 1–15.

Dinn, W.M., Harris, C.L., Aycicegi, A., Greene, P., & Andover, M.S. (2002). Positive and negative schizotypy in a student sample: Neurocognitive and clinical correlates. *Schizophrenia Research*, *56*, 171–185.

Diwadkar, V.A., Montrose, D.M., Dworakowski, D., Sweeney, J.A., & Keshavan, M.S. (2006). Genetically predisposed offspring with schizotypal features: An ultra high-risk group for schizophrenia? *Progress in Neuropsychopharmacology and Biological Psychiatry*, *30*, 230–238.

Dominguez, M.G., Wichers, M., Lieb, R., Wittchen, H.U., & van Os, J. (2011). Evidence that onset of clinical psychosis is an outcome of progressively more persistent subclinical psychotic experiences: An 8-year cohort study. *Schizophrenia Bulletin*, *37*, 84–93.

Dworkin, R., Lewis, J., Cornblatt, B., & Erlenmeyer-Kimling, L. (1994). Social competence deficits in adolescents at risk for schizophrenia. *Journal of Nervous and Mental Disease*, *182*, 103–108.

Egan, M.F., Goldberg, T.E., Kolachana, B.S., Callicott, J.H., Mazzanti, C.M., Straub, R.E., … Weinberger, D.R. (2001). Effect of COMT Val108/158 Met genotype on frontal lobe function and risk for schizophrenia. *Proceedings of the National Academy of Sciences of the United States of America*, *98*, 6917–6922.

Erlenmeyer-Kimling, L., Squires-Wheeler, E., Adamo, U.H., Bassett, A.S., Cornblatt, B.A., Kestenbaum, C.J., … Gottesman, I.I. (1995). The New York High-Risk Project. Psychoses and cluster A personality disorders in offspring of schizophrenic parents at 23 years of follow-up. *Archives of General Psychiatry*, *52*, 857–865.

Ettinger, U., Williams, S.C., Meisenzahl, E.M., Möller, H.J., Kumari, V., & Koutsouleris, N. (2011). Association between brain structure and psychometric schizotypy in healthy individuals. *World Journal of Biological Psychiatry* [Epub ahead of print].

Evans, L.H., Gray, N.S., & Snowden, R.J. (2005). Prepulse inhibition of startle and its moderation by schizotypy and smoking. *Psychophysiology*, *42*, 223–231.

Evans, L.H., Gray, N.S., & Snowden, R.J. (2007). Reduced P50 suppression is associated with the cognitive disorganisation dimension of schizotypy. *Schizophrenia Research*, *97*, 152–162.

Eysenck, H., & Eysenck, S. (1975). *Manual of the Eysenck Personality Questionnaire*. London: Hodder and Stroughton.

Fan, J., McCandliss, B.D., Sommer, T., Raz, A., & Posner, M.I. (2002). Testing the efficiency and independence of attentional networks. *Journal of Cognitive Neuroscience*, *14*, 340–347.

Faraone, S.V., Green, A.I., Seidman, L.J., & Tsuang, M.T. (2001). ''Schizotaxia'': Clinical implications and new directions for research. *Schizophrenia Bulletin*, *27*, 1–18.

Ferraro, F.R., & Okerlund, M. (1995). Implicit memory of nonclinical schizotypal individuals. *Perceptual and Motor Skills*, *80*, 371–376.

Fioravanti, M., Carlone, O., Vitale, B., Cinti, M.E., & Clare, L. (2005). A meta-analysis of cognitive deficits in adults with a diagnosis of schizophrenia. *Neuropsychology Review*, *15*, 73–95.

Fonseca-Pedrero, E., Lemos-Giráldez, S., Paíno-Piñeiro, M., Villazón-García, U., & Muñiz, J. (2010). Schizotypal traits, obsessive-compulsive symptoms, and social functioning in adolescents. *Comprehensive Psychiatry*, *51*, 71–77.

Frangou, S. (2010). Cognitive function in early onset schizophrenia: A selective review. *Frontiers in Human Neuroscience*, *3*, 79.

Garavan, H., Ross, T.J., Li, S.J., & Stein, E.A. (2000). A parametric manipulation of central executive functioning. *Cerebral Cortex*, *10*, 585–592.

Giakoumaki, S.G., Bitsios, P., & Frangou, S. (2006). The level of prepulse inhibition in healthy individuals may index cortical modulation of early information processing. *Brain Research*, *1078*, 168–170.

Giakoumaki, S.G., Roussos, P., Pallis, E.G., & Bitsios, P. (2011). Sustained attention and working memory deficits follow a familial pattern in schizophrenia. *Archives of Clinical Neuropsychology*, *26*, 687–695.

Goldberg, T.E., Saint-Cyr, J.A., & Weinberger, D.R. (1990). Assessment of procedural learning and problem solving in schizophrenic patients by Tower of Hanoi type tasks. *Journal of Neuropsychiatry and Clinical Neuroscience*, *2*, 165–173.

Goldman-Rakic, P.S. (1994). Working memory dysfunction in schizophrenia. *Journal of Neuropsychiatry and Clinical Neuroscience*, *6*, 348–357.

Gooding, D.C., Kwapil, T.R., & Tallent, K.A. (1999). Wisconsin Card Sorting Test deficits in schizotypic individuals. *Schizophrenia Research*, *40*, 201–209.

Gooding, D.C., Matts, C.W., & Rollmann, E.A. (2006). Sustained attention deficits in relation to psychometrically identified schizotypy: Evaluating a potential endophenotypic marker. *Schizophrenia Research*, *82*, 27–37.

Gooding, D.C., Tallent, K.A., & Matts, C.W. (2005). Clinical status of at-risk individuals 5 years later: Further validation of the psychometric high-risk strategy. *Journal of Abnormal Psychology*, *114*, 170–175.

Gooding, D.C., Tallent, K.A., & Matts, C.W. (2007). Rates of avoidant, schizotypal, schizoid and paranoid personality disorders in psychometric high-risk groups at 5-year follow-up. *Schizophrenia Research*, *94*, 373–374.

Gottesman, I.I., & Shields, J. (1982). *Schizophrenia: The epigenetic puzzle*. New York: Cambridge University Press.

Green, E.K., Grozeva, D., Jones, I., Jones, L., Kirov, G., Caesar, S., … Craddock, N. (2010). The bipolar disorder risk allele at CACNA1C also confers risk of recurrent major depression and of schizophrenia. *Molecular Psychiatry*, *15*, 1016–1022.

Green, M.F. (1996). What are the functional consequences of neurocognitive deficits in schizophrenia? *American Journal of Psychiatry*, *153*, 321–330.

Gruzelier, J.H. (2003). Theory, methods and new directions in the psychophysiology of the schizophrenic process and schizotypy. *International Journal of Psychophysiology*, *48*, 221–245.

Hammer, T.B., Oranje, B., Fagerlund, B., Bro, H., & Glenthøj, B.Y. (2011). Stability of prepulse inhibition and habituation of the startle reflex in schizophrenia: A 6-year follow-up study of initially antipsychotic-naive, first-episode schizophrenia patients. *International Journal of Neuropsychopharmacology*, *14*, 913–925.

Harvey, P.D. (2011). Mood symptoms, cognition, and everyday functioning: In major depression, bipolar disorder, and schizophrenia. *Innovations in Clinical Neuroscience*, *8*, 14–18.

Hazlett, E.A., Buchsbaum, M.S., Haznedar, M.M., Newmark, R., Goldstein, K.E., Zelmanova, Y., … Siever, L.J. (2008). Cortical gray and white matter volume in unmedicated schizotypal and schizophrenia patients. *Schizophrenia Research*, *101*, 111–123.

Hazlett, E.A., Buchsbaum, M.S., Zhang, J., Newmark, R.E., Glanton, C.F., Zelmanova, Y., … Siever, L.J. (2008). Frontal-striatal-thalamic mediodorsal nucleus dysfunction in schizophrenia-spectrum patients during sensorimotor gating. *Neuroimage*, *42*, 1164–1177.

Hazlett, E.A., Levine, J., Buchsbaum, M.S., Silverman, J.M., New, A., Sevin, E.M., … Siever, L.J. (2003). Deficient attentional modulation of the startle response in patients with schizotypal personality disorder. *American Journal of Psychiatry*, *160*, 621–1626.

Hazlett, E.A., Romero, M.J., Haznedar, M.M., New, A.S., Goldstein, K.E., Newmark, R.E., … Buchsbaum, M.S. (2007). Deficient attentional modulation of startle eyeblink is associated with symptom severity in the schizophrenia spectrum. *Schizophrenia Research*, *93*, 288–295.

Heinrichs, R.W., & Zakzanis, K.K. (1998). Neurocognitive deficit in schizophrenia: A quantitative review of the evidence. *Neuropsychology*, *12*, 426–445.

Henry, J.D., Bailey, P.E., & Rendell, P.G. (2008). Empathy, social functioning and schizotypy. *Psychiatry Research*, *160*, 15–22.

Henry, J.D., & Crawford, J.R. (2005). A meta-analytic review of verbal fluency deficits in schizophrenia relative to other neurocognitive deficits. *Cognitive Neuropsychiatry*, *10*, 1–33.

Heydebrand, G. (2006). Cognitive deficits in the families of patients with schizophrenia. *Current Opinions in Psychiatry*, *19*, 277–281.

Hill, S.K., Harris, M.S., Herbener, E.S., Pavuluri, M., & Sweeney, J.A. (2008). Neurocognitive allied phenotypes for schizophrenia and bipolar disorder. *Schizophrenia Bulletin*, *34*, 743–759.

Hori, H., Nagamine, M., Soshi, T., Okabe, S., Kim, Y., & Kunugi, H. (2008). Schizotypal traits in healthy women predict prefrontal activation patterns during a verbal fluency task: A near-infrared spectroscopy study. *Neuropsychobiology*, *57*, 61–69.

Hori, H., Teraishi, T., Sasayama, D., Matsuo, J., Kawamoto, Y., Kinoshita, Y., & Kunugi, H. (2012). Relationships between season of birth, schizotypy, temperament, character and neurocognition in a non-clinical population. *Psychiatry Research*, *195*, 69–75.

Jahshan, C.S., & Sergi, M.J. (2007). Theory of mind, neurocognition, and functional status in schizotypy. *Schizophrenia Research*, *89*, 278–286.

James, W. (1890). *The principles of psychology* (Vol. 1, pp. 403–404). New York: Henry Holt.

Kane, M.J., & Engle, R.W. (2002). The role of prefrontal cortex in working-memory capacity, executive attention, and general fluid intelligence: An individual-differences perspective. *Psychonomic Bulletin and Review*, *9*, 637–671.

Karayiorgou, M., & Gogos, J.A. (1997). A turning point in schizophrenia genetics. *Neuron*, *19*, 967–979.

Kendler, K.S., Gruenberg, A.M., & Strauss, J.S. (1981). An independent analysis of the Copenhagen sample of the Danish adoption study of schizophrenia, II: The relationship between schizotypal personality disorder and schizophrenia. *Archives of General Psychiatry*, *38*, 982–998.

Kendler, K.S., Lieberman, J.A., & Walsh, D. (1989). The Structured Interview for Schizotypy (SIS): A preliminary report. *Schizophrenia Bulletin*, *15*, 559–571.

Kendler, K.S., McGuire, M., Gruenberg, A.M., O'Hare, A., Spellman, M., & Walsh, D. (1993). The Roscommon Family Study. I. Methods, diagnosis of probands, and risk of schizophrenia in relatives. *Archives of General Psychiatry*, *50*, 527–540.

Kendler, K.S., Ochs, A.L., Gorman, A.M., Hewitt, J.K., Ross, D.E., & Mirsky, A.F. (1991). The structure of schizotypy: A pilot multitrait twin study. *Psychiatry Research*, *36*, 19–36.

Kéri, S., & Janka, Z. (2004). Critical evaluation of cognitive dysfunctions as endophenotypes of schizophrenia. *Acta Psychiatrica Scandinavica*, *110*, 83–91.

Kerns, J.G., & Becker, T.M. (2008). Communication disturbances, working memory, and emotion in people with elevated disorganized schizotypy. *Schizophrenia Research*, *100*, 172–180.

Kim, M.S., Oh, S.H., Hong, M.H., & Choi, D.B. (2011). Neuropsychologic profile of college students with schizotypal traits. *Comprehensive Psychiatry*, *52*, 511–516.

Kirrane, R.M., & Siever, L.J. (2000). New perspectives on schizotypal personality disorder. *Current Psychiatry Reports*, *2*, 62–66.

Kraepelin, E. (1913). *Dementia praecox and paraphrenia*. Edinburgh: E & S Livingston.

Kumari, V., Antonova, E., & Geyer, M.A. (2008). Prepulse inhibition and "psychosis-proneness" in healthy individuals: An fMRI study. *European Psychiatry*, *23*, 274–280.

Kumari, V., Antonova, E., Geyer, M.A., ffytche, D., Williams, S.C., & Sharma, T. (2007). A fMRI investigation of startle gating deficits in schizophrenia patients treated with typical or atypical antipsychotics. *International Journal of Neuropsychopharmacology*, *10*, 463–477.

Kumari, V., Fannon, D., Sumich, A.L., & Sharma, T. (2007). Startle gating in antipsychotic-naïve first episode schizophrenia patients: One ear is better than two. *Psychiatry Research*, *151*, 21–28.

Kumari, V., Gray, J.A., Geyer, M.A., ffytche, D., Soni, W., … Sharma, T. (2003). Neural correlates of tactile prepulse inhibition: A functional MRI study in normal and schizophrenic subjects. *Psychiatry Research*, *122*, 99–113.

LaPorte, D.J., Kirkpatrick, B., & Thaker, G.K. (1994). Psychosis-proneness and verbal memory in a college student population. *Schizophrenia Research*, *12*, 237–445.

Laws, K.R. (1999). A meta-analytic review of Wisconsin Card Sort studies in schizophrenia: General intellectual deficit in disguise? *Cognitive Neuropsychiatry*, *4*, 1–30.

Laws, K.R., Patel, D.D., & Tyson, P.J. (2008). Awareness of everyday executive difficulties precede overt executive dysfunction in schizotypal subjects. *Psychiatry Research*, *160*, 8–14.

Laurent, A., Duly, D., Murry, P., Foussard, N., Boccara, S., Mingat, F., … d'Amato, T. (2001). WCST performance and schizotypal features in the first-degree relatives of patients with schizophrenia. *Psychiatry Research*, *104*, 133–144.

Lee, J., & Park, S. (2005). Working memory impairments in schizophrenia: A meta-analysis. *Journal of Abnormal Psychology*, *114*, 599–611.

Lenzenweger, M.F., Cornblatt, B.A., & Putnick, M. (1991). Schizotypy and sustained attention. *Journal of Abnormal Psychology*, *100*, 84–89.

Lenzenweger, M.F., & Gold, J.M. (2000). Auditory working memory and verbal recall memory in schizotypy. *Schizophrenia Research*, *42*, 101–110.

Lenzenweger, M.F., & Korfine, L. (1994). Perceptual aberrations, schizotypy, and the Wisconsin Card Sorting Test. *Schizophrenia Bulletin*, *20*, 345–357.

Le Pelley, M.E., Schmidt-Hansen, M., Harris, N.J., Lunter, C.M., & Morris, C.S. (2010). Disentangling the attentional deficit in schizophrenia: Pointers from schizotypy. *Psychiatry Research*, *176*, 143–149.

Lewandowski, K.E., Barrantes-Vidal, N., Nelson-Gray, R.O., Clancy, C., Kepley, H.O., & Kwapil, T.R. (2006). Anxiety and depression symptoms in psychometrically identified schizotypy. *Schizophrenia Research*, *83*, 225–235.

Li, T., Ma, X., Sham, P.C., Sun, X., Hu, X., Wang, Q., … Collier, D.A. (2004). Evidence for association between novel polymorphisms in the PRODH gene and schizophrenia in a Chinese population. *American Journal of Medical Genetics. Part B, Neuropsychiatric Genetics*, *129B*, 13–15.

Light, G.A., & Braff, D.L. (2001). Measuring P50 suppression and prepulse inhibition in a single recording session. *American Journal of Psychiatry*, *158*, 2066–2068.

Linney, Y.M., Murray, R.M., Peters, E.R., MacDonald, A.M., Rijsdijk, F., & Sham, P.C. (2003). A quantitative genetic analysis of schizotypal personality traits. *Psychological Medicine*, *33*, 803–816.

Linscott, R.J., Marie, D., Arnott, K.L., & Clarke, B.L. (2006). Over-representation of Maori New Zealanders among adolescents in a schizotypy taxon. *Schizophrenia Research*, *84*, 289–296.

Liu, H., Heath, S.C., Sobin, C., Roos, J.L., Galke, B.L., Blundell, M.L., … Karayiorgou, M. (2002). Genetic variation at the 22q11

PRODH2/DGCR6 locus presents an unusual pattern and increases susceptibility to schizophrenia. *Proceedings of the National Academy of Sciences of the United States of America*, *99*, 3717–3722.

Ludewig, K., Geyer, M.A., & Vollenweider, F.X. (2003). Deficits in prepulse inhibition and habituation in never-medicated, first-episode schizophrenia. *Biological Psychiatry*, *54*, 121–128.

Ma, X., Sun, J., Yao, J., Wang, Q., Hu, X., Deng, W., … Li, T. (2007). A quantitative association study between schizotypal traits and COMT, PRODH and BDNF genes in a healthy Chinese population. *Psychiatry Research*, *153*, 7–15.

Mackeprang, T., Kristiansen, K.T., & Glenthoj, B.Y. (2002). Effects of antipsychotics on prepulse inhibition of the startle response in drug-naïve schizophrenic patients. *Biological Psychiatry*, *52*, 863–873.

Mannan, M.R., Hiramatsu, K.I., Hokama, H., & Ohta, H. (2001). Abnormalities of auditory event-related potentials in students with schizotypal personality disorder. *Psychiatry and Clinical Neurosciences*, *55*, 451–457.

Mason, O., Claridge, G., & Jackson, M. (1995). New scales for the assessment of schizotypy. *Personality and Individual Differences*, *18*, 7–13.

Matheson, S., & Langdon, R. (2008). Schizotypal traits impact upon executive working memory and aspects of IQ. *Psychiatry Research*, *159*, 207–214.

Matsui, M., Sumiyoshi, T., Kato, K., Yoneyama, E., & Kurachi, M. (2004). Neuropsychological profile in patients with schizotypal personality disorder or schizophrenia. *Psychology Report*, *94*, 387–397.

Matsui, M., Suzuki, M., Zhou, S.Y., Takahashi, T., Kawasaki, Y., Yuuki, H., … Kurachi, M. (2008). The relationship between prefrontal brain volume and characteristics of memory strategy in schizophrenia spectrum disorders. *Progress in Neuropsychopharmacology and Biological Psychiatry*, *32*, 1854–1862.

Matsui, M., Yuuki, H., Kato, K., Takeuchi, A., Nishiyama, S., Bilker, W.B., & Kurachi, M. (2007). Schizotypal disorder and schizophrenia: A profile analysis of neuropsychological functioning in Japanese patients. *Journal of the International Neuropsychological Society*, *13*, 672–682.

Meehl, P.E. (1989). Schizotaxia revisited. *Archives of General Psychiatry*, *46*, 935–944.

Miller, B.L., & Cummings, J.L. (2007). *The human frontal lobes: Functions and disorders* (2nd ed., p. 27). New York: Guilford Press.

Miyake, A., Friedman, N.P., Emerson, M.J., Witzki, A.H., Howerter, A., & Wager, T.D. (2000). The unity and diversity of executive functions and their contributions to complex "Frontal Lobe" tasks: A latent variable analysis. *Cognitive Psychology*, *41*, 49–100.

Noguchi, H., Hori, H., & Kunugi, H. (2008). Schizotypal traits and cognitive function in healthy adults. *Psychiatry Research*, *161*, 162–169.

Obiols, J.E., Clos, M., Corberó, E., García-Domingo, M., de Trinchería, I., & Doménech, E. (1992). Sustained attention deficit in young schizophrenic and schizotypic men. *Psychological Reports*, *71*, 1131–1136.

Palmer, B.W., & Heaton, R.K. (2000). Executive dysfunction in schizophrenia. In T. Sharma & P.D. Harvey (Eds.), *Cognition in schizophrenia: Impairments, importance and treatment strategies*, (pp. 51–72). Oxford: Oxford University Press.

Park, S., Holzman, P.S., & Lenzenweger, M.F. (1995). Individual differences in spatial working memory in relation to schizotypy. *Journal of Abnormal Psychology*, *104*, 355–363.

Park, S., & McTigue, K. (1997). Working memory and the syndromes of schizotypal personality. *Schizophrenia Research*, *26*, 213–220.

Poulton, R., Caspi, A., Moffitt, T.E., Cannon, M., Murray, R., & Harrington, H. (2000). Children's self-reported psychotic symptoms and adult schizophreniform disorder: A 15-year longitudinal study. *Archives of General Psychiatry*, *57*, 1053–1058.

Raine, A. (1991). The SPQ: A scale for the assessment of schizotypal personality based on DSMIII-R criteria. *Schizophrenia Bulletin*, *17*, 555–564.

Raine, A. (2006). Schizotypal personality: Neurodevelopmental and psychosocial trajectories. *Annual Review of Clinical Psychology*, *2*, 291–326.

Roussos, P., Giakoumaki, S.G., & Bitsios, P. (2009). A risk PRODH haplotype affects sensorimotor gating, memory, schizotypy, and anxiety in healthy male subjects. *Biological Psychiatry*, *65*, 1063–1070.

Roussos, P., Giakoumaki, S.G., Georgakopoulos, A., Robakis, N.K., & Bitsios, P. (2011). The CACNA1C and ANK3 risk alleles impact on affective personality traits and startle reactivity but not on cognition or gating in healthy males. *Bipolar Disorders*, *13*, 250–259.

Schell, A.M., Dawson, M.E., Hazlett, E.A., & Filion, D.L. (1995). Attentional modulation of startle in psychosis-prone college students. *Psychophysiology*, *32*, 266–273.

Schérer, H., Stip, E., Paquet, F., & Bédard, M.A. (2003). Mild procedural learning disturbances in neuroleptic-naive patients with schizophrenia. *Journal of Neuropsychiatry and Clinical Neuroscience*, *15*, 58–63.

Schürhoff, F., Szöke, A., Chevalier, F., Roy, I., Méary, A., Bellivier, F., … Leboyer, M. (2007). Schizotypal dimensions: An intermediate phenotype associated with the COMT high activity allele. *American Journal of Medical Genetics. Part B, Neuropsychiatric Genetics*, *144B*, 64–68.

Schwarzkopf, S.B., Lamberti, J.S., & Smith, D.A. (1993). Concurrent assessment of acoustic startle and auditory P50 evoked potential measures of sensory inhibition. *Biological Psychiatry*, *33*, 815–828.

Seghers, J.P., McCleery, A., & Docherty, N.M. (2011). Schizotypy, alexithymia, and socioemotional outcomes. *Journal of Nervous and Mental Disease*, *199*, 117–121.

Sheldrick, A.J., Krug, A., Markov, V., Leube, D., Michel, T.M., Zerres, K., … Kircher, T. (2008). Effect of COMT val158met genotype on cognition and personality. *European Psychiatry*, *23*, 385–389.

Siever, L.J., & Davis, K.L. (2004). The pathophysiology of schizophrenia disorders: Perspectives from the spectrum. *American Journal of Psychiatry*, *161*, 398–413.

Simons, R.F., & Giardina, R.D. (1992). Reflex modification in psychosis-prone young adults. *Psychophysiology*, *29*, 8–16.

Skodol, A.E., Gunderson, J.G., McGlashan, T.H., Dyck, I.R., Stout, R.L., Bender, D.S., … Oldham, J.M. (2002). Functional impairment in patients with schizotypal, borderline, avoidant, or obsessive-compulsive personality disorder. *American Journal of Psychiatry*, *159*, 276–283.

Smyrnis, N., Avramopoulos, D., Evdokimidis, I., Stefanis, C.N., Tsekou, H., & Stefanis, N.C. (2007). Effect of schizotypy on cognitive performance and its tuning by COMT val158 met genotype variations in a large population of young men. *Biological Psychiatry*, *61*, 845–853.

Spaulding, W., Garbin, C.P., & Dras, S.R. (1989). Cognitive abnormalities in schizophrenic patients and schizotypal college students. *Journal of Nervous and Mental Disease*, *177*, 717–728.

Spitznagel, M.B., & Suhr, J.A. (2002). Executive function deficits associated with symptoms of schizotypy and obsessive-compulsive disorder. *Psychiatry Research*, *110*, 151–163.

Squire, L.R., & Zola, S.M. (1996). Structure and function of declarative and nondeclarative memory systems. *Proceedings of the National Academy of Sciences of the United States of America*, *93*, 13515–13522.

Startup, M. (1999). Schizotypy, dissociative experiences and childhood abuse: Relationships among self-report measures. *British Journal of Clinical Psychology*, *38*, 333–344.

Steel, C., Marzillier, S., Fearon, P., & Ruddle, A. (2009). Childhood abuse and schizotypal personality. *Social Psychiatry and Psychiatric Epidemiology*, *44*, 917–923.

Stefanis, N.C., Trikalinos, T.A., Avramopoulos, D., Smyrnis, N., Evdokimidis, I., Ntzani, E.E., … Stefanis, C.N. (2007). Impact of schizophrenia candidate genes on schizotypy and cognitive endophenotypes at the population level. *Biological Psychiatry*, *62*, 784–792.

Stefanis, N.C., Trikalinos, T.A., Avramopoulos, D., Smyrnis, N., Evdokimidis, I., Ntzani, E.E., … Stefanis, C.N. (2008). Association of RGS4 variants with schizotypy and cognitive endophenotypes at the population level. *Behavior and Brain Function*, *4*, 46.

Stefanopoulou, E., Manoharan, A., Landau, S., Geddes, J.R., Goodwin, G., & Frangou, S. (2009). Cognitive functioning in patients with affective disorders and schizophrenia: A meta-analysis. *International Review of Psychiatry*, *21*, 336–356.

Strauss, E., Sherman, E.M.S., & Spreen, O. (2006). *A compendium of neuropsychological tests: Administration, norms and commentary* (3rd ed). New York: Oxford University Press.

Stuss, D.T., & Alexander, M.P. (2000). Executive functions and the frontal lobes: A conceptual view. *Psychological Research*, *63*, 289–298.

Suhr, J.A. (1997). Executive functioning deficits in hypothetically psychosis-prone college students. *Schizophrenia Research*, *27*, 29–35.

Suhr, J.A., & Spitznagel, M.B. (2001). Factor versus cluster models of schizotypal traits. II: Relation to neuropsychological impairment. *Schizophrenia Research*, *52*, 241–250.

Sumich, A., Kumari, V., Gordon, E., Tunstall, N., & Brammer, M. (2008). Event-related potential correlates of paranormal ideation and unusual experiences. *Cortex*, *44*, 1342–1352.

Swerdlow, N.R., Filion, D., Geyer, M.A., & Braff, D.L. (1995). "Normal" personality correlates of sensorimotor, cognitive, and visuospatial gating. *Biological Psychiatry*, *37*, 286–299.

Takahashi, H., Iwase, M., Canuet, L., Yasuda, Y., Ohi, K., Fukumoto, M., … Takeda, M. (2010). Relationship between prepulse inhibition of acoustic startle response and schizotypy in healthy Japanese subjects. *Psychophysiology*, *47*, 831–837.

Tallent, K.A., & Gooding, D.C. (1999). Working memory and Wisconsin Card Sorting Test performance in schizotypic individuals: A replication and extension. *Psychiatry Research*, *89*, 161–170.

Thaker, G., Adami, H., & Gold, J. (2001). Functional deterioration in individuals with schizophrenia spectrum personality symptoms. *Journal of Personality Disorders*, *15*, 229–234.

Thaker, G.K. (2008). Neurophysiological endophenotypes across bipolar and schizophrenia psychosis. *Schizophrenia Bulletin*, *34*, 760–773.

Trestman, R.L., Horvath, T., Kalus, O., Peterson, A.E., Coccaro, E., Mitropoulou, V., … Siever, L.J. (1996). Event-related potentials in schizotypal personality disorder. *Journal of Neuropsychiatry and Clinical Neurosciences*, *8*, 33–40.

Turetsky, B.I., Calkins, M.E., Light, G.A., Olincy, A., Radant, A.D., & Swerdlow, N.R. (2007). Neurophysiological endophenotypes of schizophrenia: The viability of selected candidate measures. *Schizophrenia Bulletin*, *33*, 69–94.

van Os, J., Linscott, R.J., Myin-Germeys, I., Delespaul, P., & Krabbendam, L. (2009). A systematic review and meta-analysis of the psychosis continuum: Evidence for a psychosis proneness-persistence-impairment model of psychotic disorder. *Psychological Medicine*, *39*, 179–195.

Venables, P.H. (1996). Schizotypy and maternal exposure to influenza and to cold temperature: The Mauritius study. *Journal of Abnormal Psychology*, *105*, 53–60.

Wager, T.D., & Smith, E.E. (2003). Neuroimaging studies of working memory: A meta-analysis. *Cognitive, Affective and Behavioral Neuroscience*, *3*, 255–274.

Welham, J., Scott, J., Williams, G., Najman, J., Bor, W., O'Callaghan, M., & McGrath, J. (2009). Emotional and behavioural antecedents of young adults who screen positive for non-affective psychosis: A 21-year birth cohort study. *Psychological Medicine*, *39*, 625–634.

Whyte, M.C., McIntosh, A.M., Johnstone, E.C., & Lawrie, S.M. (2005). Declarative memory in unaffected adult relatives of patients with schizophrenia: A systematic review and meta-analysis. *Schizophrenia Research*, *78*, 13–26.

Yasuda, Y., Hashimoto, R., Ohi, K., Fukumoto, M., Umeda-Yano, S., Yamamori, H., … Takeda, M. (2011). Impact on schizotypal personality trait of a genome-wide supported psychosis variant of the ZNF804A gene. *Neuroscience Letters*, *495*, 216–220.