Dissociating Response Prepotency and Response Conflict within Tasks of Action Inhibition

among Individuals Scoring High on the Schizotypal Personality Questionnaire

by

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I hereby declare that I am the sole author of this thesis. This is a true copy of the thesis, including any required final revisions, as accepted by my examiners.

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Abstract

Theories embedded within evolutionary neurobiology offer useful frameworks within which to understand cognitive impairment in schizophrenia (SCZ). The current research invokes the Dual Trends Theory (DTT), an evolutionary model that posits that neural architecture develops along two separate pathways: the dorsal 'archicortical' trend and the ventral 'paleocortical' trend. Although various lines of research converge to suggest that SCZ is associated with dorsal trend impairment in the context of relative ventral trend sparing, one persistent inconsistency exists. Specifically, individuals with SCZ routinely show impairment on tasks of action inhibition (AI; the ability to inhibit a pre-planned movement), a function routinely shown to be mediated by the inferior frontal gyrus, a key structure of the ventral trend. Here we argue that conventional tasks of AI conflate AI *per se* with response conflict (CON) demands, a function shown to be mediated by the anterior cingulate cortex, a key structure of the dorsal trend. We define CON as any aspect of a task that increases the difficulty of deciphering or interpreting the meaning of task stimuli (e.g., greater perceptual similarity between imperative task stimuli). The current research administered novel AI tasks in order to independently examine increases in CON and increases in the prepotency to respond to a pre-planned movement (PREP; considered a more fundamental measure of AI). Consistent with study hypotheses, individuals with Schizoprenia-spectrum disorders (specifically schizotypy) failed to show compensatory response time (RT) slowing when confronted with increasing CON demands yet showed proportional RTs, relative to healthy control participants, as PREP demands increased. These findings were interpreted as reflecting impairment in their ability to detect and/or decipher CON. More broadly, these findings suggest that cognitive abnormalities in SCZ may represent disproportionately impaired dorsal trend circuitry.

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"The facts are always friendly, every bit of evidence one can acquire, in any area, leads one that much closer to what is true."- Carl Rogers.

Dedication

This dissertation is dedicated to my dear friend, Rachel Rae, whose energy and creativity I will greatly miss. We'll always have Paris.

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List of Abbreviations

ACC: Anterior Cingulate Cortex

AI: Action Inhibition

AIT: Action Inhibition Task

AIT-R: Action Inhibition Task-Revised

ANOVA: Analysis of Variance

AX-CPT: The AX version of the CPT

CC: Cognitive Control

COMT: Catechol-O-Methyl transferase (O denotes oxygen)

CON: Response Conflict

DA: Dopamine

df: Degrees of Freedom

DLPFC: Dorsolateral Prefrontal Cortex

DPM: Dual Processing Model of Vision

DOH: Dual Origins Hypothesis

DTT: Dual Trends Theory

DSM-IV: Fouth Edition of the Diagnostic and Statistical Manual for Mental Disorders

ERP: Event-Related Potentials

fMRI: Functional Magnetic Resonance Imaging

FSIQ: Full Scale Intelligence Quotient

HKRT: Home Key Release Time

hiCON: High Response Conflict Difficulty

hiPREP: High Response Prepotency Difficulty

HKRT_INH: HKRT on INH trials

SU HKRT: HKRT on SU trials

IFG: Inferior Frontal Gyrus

IGT: Iowa Gambling Task

INH: Inhibition Trial in Action Inhibition Task (Study 1)

INH HKRT: HKRTS in INH Trials

loCON: Low Response Conflict Difficulty

loPREP: Low Response Prepotency Difficulty

MAM: Methyl Azoxymethanol Acetate

min.: Minutes

msec: Milliseconds

NA: Nucleus Accumbens

NEO-FFI: NEO Five Factor Inventory

NEO-PI-R: NEO Personality Inventory-Revised

NVHL: Neonatal Ventral Hippocampal Lesion Model

OAT: Object Alternation Task

OFC: Orbital Frontal Cortex

PAIsf: Short Form of the Personality Assessment Inventory

PDSQ: Psychiatric Diagnostic Screening Questionnaire

PFC: Prefrontal Cortex

PREP: Response Prepotency

PV: Peak Velocity

RM-ANOVA: Repeated Measures ANOVA

SCZ: Schizophrenia

sec: Seconds

SOA: Stimulus-Onset Asynchrony

SPQ: Schizotypal Personality Questionnaire

SPQ-B: Schizotypal Personality Questionnaire-form B (shortened form)

SSD: Stop-Signal Delay

SSP: Stop-Signal Paradigm

SSRT: Stop-Signal Reaction Time

SU: Speed-Up Trial on Action Inhibition Task (Study 1)

SU HKRT: HKRTs in SU trials

SURT: Response time on SU trial

TTPV: Time to Peak Velocity

VH: Ventral Hippocampus

VLPFC: Ventrolateral Prefrontal Cortex

WCST: Wisconsin Card Sorting Task

Organization of Dissertation

The current dissertation contains two freestanding research papers (*Study 1* and *Study 2*) which are preceded by a lengthier and detailed *General Introduction* and followed by a more extensive *General Discussion*. This chosen format has resulted in some redundancy between sections. In particular, there is substantial overlap between elements of the *General Discussion* and the discussion sections for each independent research paper. Hopefully this explanation provides a coarse roadmap by which the reader can approach this material with his/her desired balance between efficiency and comprehensiveness realized.

General Introduction

Cognitive impairment in schizophrenia

Cognitive impairment among individuals with Schizophrenia (SCZ) is considered a core deficit of the disorder (American Psychiatric Association, 1994). Various reviews reveal cognitive dysfunction among persons with SCZ across all ability domains measured by clinical neuropsychological tests (Aleman, Hijman, de Haan, and Kahn, 1999; Heinrichs & Zakzanis, 1998; O'Carroll, 2000; O'Donnell, 2007). In a large comprehensive meta-analysis, Heinrichs & Zakzanis (1998) found evidence of impairment in attention and concentration (Braff, 1993; Cornblatt & Keilp, 1994), cognitive flexibility and abstraction (Gruzelier, Seymour, Wilson, Jolley, & Hirsch, 1988; Heinrichs, 1990; Van der Does & Van den Bosch, 1992; Weinberger, Berman, & Illowsky, 1988), manual dexterity (Goldstein & Zubin, 1990; Schwartz, Carr, Munich, Bartuch, Lesser, Rescigno, Viegener, & 1990), visuospatial performance (Green & Walker, 1985; Raine, 1992; Stuss, Benson, Kaplan, Weir, Naeser, Lieberman, & Ferrill, 1983), verbal skill (Barr, Bilder, Goldberg, Kaplan, & Mukherjee, 1989), memory acquisition (Goldberg, Gold, Greenberg, Griffin, Schulz, Pickar, Kleinman, & Weinberger, 1993). Paulsen, Heaton, Sadek, Perry, Delis, Braff, Kuck, Zisook, & Jeste, 1995), and delayed recall (Randolph, Gold, Kozora, Cullum, Herman, & Wyler, 1994; Saykin, Gur, Gur, Mozley, Mozley, Resnick, Kester, & Stafiniak, 1991). The largest effect sizes were observed within the domains of verbal memory, motor, and attentional/executive functioning, providing evidence for selective deficits within these domains. Thus, the cognitive profile among persons with SCZ can be characterized as one of disproportionate impairment in memory, learning and executive function within the context of broad cognitive impairment (Heinrichs & Zakzanis, 1998).

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Cognitive impairment among individuals with SCZ has been shown to have a stable course, persisting from early childhood, through the first psychotic episode and into chronic phases (Bilder, 1997). Thus, cognitive deficits appear to manifest well before the onset of psychosis, and subsequent diagnosis of SCZ. The course among elderly SCZ patients appears more variable, yet remains relatively stable for the majority of individuals with this diagnosis (Harvey et al., 1999; Kurt, 2005). Among chronically institutionalized elderly individuals with SCZ 30% of patients were observed to show significant worsening of cognitive and functional status, whereas only 7% experienced improvement. Lower levels of education and more severe positive symptoms at baseline predicted increased risk of decline (Harvey, Parrella, White, Mohs, Davidson, & Davis, 1999). In conducting a power analysis of longitudinal studies published since 1997, Kurt (2005) found evidence of two distinct cognitive trajectories during the lifespan in persons with SCZ. Overall measures of IQ and gross cognitive status showed deterioration comparable to benign aging. Specific measures of cognition were remarkably consistent across ages, regardless of whether patients were in their first episode of illness or chronic. In contrast, middle-aged and elderly institutionalized patients with SCZ showed decline in gross measures of cognitive status even over a brief 2 ½ year test-retest interval in patients 65 or older. These findings were interpreted as potentially representing manifestations of distinct pathophysiological mechanisms of the illness during different phases of the disease.

In terms of its prognostic value, cognitive impairment has been shown to be predictive of functional outcome (Tabaras-Seisdedos, Balanza-Martinez, Sanchez-Moreno, Martinex-Aran, Salazar-Fraile, Selva-Vera, Rubio, Mata, Gomez-Beneyto, & Vieta, 2008; Tamminga et al., 1998; Green, Kern, & Heaton, 2004). In contrast, psychotic symptoms (in particular positive symptoms) appear to be relatively less predictive of occupational and social functioning (Green,

Kern, Braff & Mintz, 2000; Tabaras-Seisdedos et al., 2008). Cognitive impairment has also been

shown to be moderately correlated with negative symptoms (less so with positive symptoms), as

well as poor premorbid functioning (Addington & Addington, 2008; Andreasen, Flaum, Swayze,

Tyrrel, & Arndt, 1990).

Given the importance and persistence of cognitive impairment in persons with SCZ,

scientists have been eager to understand its neurobiological underpinnings. However, despite

progress in characterizing the nature of the cognitive deficits, the search for an underlying

biological mechanism remains somewhat elusive. Presently, our understanding of the

functional neurobiology of SCZ largely derives from traditional neuropsychological models of

acquired brain damage (e.g., traumatic brain injury, tumours, stroke). Within such

frameworks, brain function is inferred through correlating behavioral change with

circumscribed regions of brain damage. Thus, the presence of brain damage tests the validity

of lesion-based theories by establishing whether they result in deficits corresponding to the

hypothesized function (Stuss & Levine, 2002).

Although helpful in localizing lesions and predicting the behavioural consequences of

lesions among individuals with acquired brain pathology, traditional neuropsychological

models have been less able to reliably describe and characterize the neuropathology of

neurodevelopmental disorders such as SCZ. For example, although various researchers focus

their investigations on similarities between persons with SCZ and those with frontal or

temporal lobe lesions (Goldberg & Weinberger, 1988; Levin, 1984; Robinson, 1997)

experimental data demonstrate that these patients often differ significantly across measures of

symptomatology and cognition (Gron, 1998; Matsushima, Kojima, Ohbayashi, Ando, Ando, &

Shimazono, 1992; Pantelis, Barber, Barnes, Nelson, Owen, & Robbins, 1999; Fuhii & Ahmed,

2002). Second, neuropathological investigations of individuals with SCZ fail to reveal obvious macroscopic lesions or pathology (Freeman & Karson, 1993; Hirsch, Hoglinger, Rousselet, Breidert, Parain, Feger, Ruberg, Prigent, Cohen-Salmon, & Launay, 2003; Pepeu, Casamenti, Pedata, Cosi, & Pepeu, 1986). Instead, the pathology of SCZ is characterized by subtle, cellular pathological abnormalities distributed across wider neural systems (Benes, Kwok, Vincent, & Todtenkoft, 1998; Harrison, Everitt, & Robbins, 1999; Nemeroff, Musselman, Nathan, Schatzberg, Knable, & Kleinman, 1997; Wong & Van Tol, 2003). Finally, SCZ, as well as many forms of psychopathology, appear to be neurodevelopmental in nature, rather than acquired in adulthood (Dawson, Frey, Panagiotides, Osterling, & Hessl, 1997; Goodman & Gotlib, 1999; Graham, Heim, Goodman, Miller, & Nemeroff, 1999; Harrison, 1997; Palomo, Archer, Kostrzewa, Beninger, 2004 Waddington, Torrey, Crow, & Hirsch, 1991); thus, their observed neurobiological abnormalities emerge during early development, then interact with ones' subsequent experience, to produce psychopathology. Collectively, these limitations highlight the need for neurobiological models that can explain the diversity of cognitive and symptom profiles, widespread neuropathology, and developmental abnormalities associated with SCZ (Christensen & Bilder, 2000).

Theories based on evolutionary neurobiology offer an alternate conceptual framework within which the anomalous functional brain organization that characterizes SCZ can be understood. Natural selection, a primary tenet of evolutionary biology (Gould 1992), provides a rationale as to why certain brain structures have evolved and persisted over time as well as why new structures have evolved. More succinctly, brain regions have been "selected for" based on their behavioural usefulness or adaptive role. Evolutionary biologists, including neuroecologists, seek to understand why new structures and functions have evolved via the

expansion and differentiation of brain structures across evolution (for review, see Sherry, 2006). Exploring evolutionary expansion of the brain provides a window into its functional brain organization and holds the promise of uncovering underlying neural mechanisms of illness where development has gone awry (Gould, 1977). Various researchers have invoked evolutionary theory as a means of understanding anomalous brain functioning in SCZ (Crow, 1995; Khaitovich, Lockstone, Wayland, Tsang, Jayatilaka, Guo, Zhou, et al., 2008; for review, see Burns, 2004). The current thesis is grounded in this tradition, whereby cognitive functioning among individuals with SCZ-spectrum disorders can be understood within an evolutionary framework.

The Dual Trends Theory

The Dual Trends Theory (DTT), has been proposed as an appropriate evolutionary model from which impaired brain functioning in SCZ can be better understood (Christensen & Bilder, 2000; Giaccio, 2006). The DTT was originally based on comparative phylogenetic studies of cortical expansion/differentiation and cytoarchitectonic development and organizes brain anatomy and function into two separate neural systems (Sanides, 1972). In this model, all cortical brain regions are believed to have evolved from two more primitive areas, or prime moieties. For instance, cortical areas arising from the amygdala and adjacent olfactory cortex comprise the paleocortical or ventral trend while cortical areas arising from hippocampal-induseal moiety form the archicortical or dorsal trend (Pandya & Yeterian, 1985). These two systems consist of various lines of development radiating outward from its limbic core (i.e., the amygdala and the hippocampus). Projections within these pathways reflect the successive stages of cytoarchitectonic development (Pandya, Seltzer, & Barbas, 1988). For example, proceeding from phylogenetically 'older' to 'newer' areas, pathways begin within the

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allocortex, the three-layered configuration in the primordial limbic zones (i.e., amygdala and hippocampus) to the transitional periallocortical and proisocortical stages (paralimbic areas). Projections from paralimbic structures extend to the most fully developed, 6-layered, cortex, referred to as the isocortex or neocortex (Pandya et al., 1988). In the dorsal trend, for example, projections for the hippocampus (prime moiety) extend to the parahippocampal gyrus (periallocortex), then on to the anterior cingulate cortex (ACC; allocortex), and the dorsolateral prefrontal cortex (DLFC; isocortex) (Pandya et al., 1988).

With regard to function, the dorsal trend is generally thought to sub-serve volitional, goal-directed behaviour that is both conscious and stable while the ventral trend is thought to mediate the phasic interruption of ongoing goal-directed behaviour in response to novel environmental events that have emotional or motivational significance (Christensen & Bilder, 2000; Giaccio, 2006). The anatomical and functional duality of these trends leaves open the possibility that damage to one system may result in a selective, disproportionate impairment in functions mediated by that trend with relative sparing of functions mediated by the unaffected system. Of note, Giaccio (2006) has also applied this dual trend framework to conceptualize abnormalities in functional brain organization that lead to an array of psychiatric illnesses, a model he coins, The Dual Origins Hypothesis (DOH).

Dual trend frameworks have also been invoked to understand neural functioning more broadly. In a comprehensive review of frontal lobe functioning, Stuss & Levine (2002) also argue for the existence of two functionally distinct areas within primate frontal lobes. Similar to Christensen & Bilder (2000) and Giaccio (2006), Stuss & Levine (2002) cite the evolutionary theory of cortical architectonics initially described by Pandya and colleagues (e.g., Pandya & Yeterian, 1969) as the basis for the functional dissociablility of the dorsal and

ventral aspects of the frontal lobes. Consistent with the DTT and DOH, Stuss & Levine (2002) conclude that DLPFC structures within the frontal lobes mediate executive functioning, such as spatial and conceptual reasoning processes, while the ventral prefrontal cortex (VPFC) mediates behavioural self-regulations, as evidenced by its role in inhibition, emotion, and reward processing (Stuss & Levine, 2002).

Pribram and McGuiness' (1975) model of attentional control also posits a similar dual systems framework; separable neural pathways that underlie unique stimulus response modes labelled the 'arousal' and 'activation' system, respectively. The arousal system is highly phasic, potentiated by novel and salient environmental stimuli but attenuated by repetitive, redundant stimuli. Neural activity within the activation system is less sensitive to perturbations from environmental stimuli and is instead potentiated by redundant, stable stimuli. The activation system thereby primes the organism for postural readiness and motivationally directed action (McGuiness & Pribram, 1980; Pribram & McGuiness, 1975) while the arousal system serves to interrupt ongoing action in order that novel events can be evaluated for their motivational significance and acted upon accordingly. As such, the activation system can be conceptualized as analogous to the dorsal trend while the arousal system converges with characterizations of the ventral trend.

Schizophrenia: disproportionate deficits in dorsal trend

Researchers have suggested that within the DTT model, SCZ-related cognitive and behavioural impairment can be conceptualized as reflecting disproportionate dysfunction of the dorsal trend, in the context of relative sparing of the ventral pathway (Christensen & Bilder, 2000; Giaccio, 2006). This observation is borne out in various lines of neurobiological and behavioural research, which are reviewed below.

<u>Neurobiological evidence of disproportionate dysfunction in dorsal trend</u>

Grace's model of hippocampal functioning in SCZ. Grace's neural model (2000) of

SCZ also implicates dorsal trend structures (i.e., hippocampus) as a basis for the behavioural

abnormalities associated with SCZ. Grace (2000) posits that under conditions of normal

hippocampal functioning, the hippocampus provides contextual or memorial information to

behavioural programs selected by the NA among those provided by the PFC to select

behavioural output from among multiple motor plans provided via prefrontal afferents.

Importantly, in conditions where a stimulus of high affective valence is introduced (e.g., a

threat) the amygdala has the capacity to override hippocampal influence and redirect behaviour

in a fashion expected to deal with the threatening stimulus. According to this model, the

hippocampi of individuals with SCZ are unable to provide necessary contextual constraints,

thereby leaving affective amygdala input un-gated or un-tempered. At the behavioural level,

the absence of contextual constraints biases the individual to react based disproportionately on

affective information. Grace (2000) argues that such a mechanism may cause a flooding of

emotions and the inability to discriminate relevant and irrelevant stimuli, features

characteristically present in individuals with SCZ.

Hippocampal gating of amygdalar activation occurs at the level of the nucleus

accumbens (NA), a central component of the basal ganglia (see Grace, 2000 for review). The

NA integrates signals from limbic and cortical areas to modulate motor activity in relation to

goal-directed behaviour (Groenewegen, Wright, & Beiher, 1996). The amygdala provides the

NA with emotional and affective input (Davidson, 2002; Gallagher & Chiba, 1996). Of

greatest significance to SCZ, is the input received from the basolateral nuclei of the amygdala

(BLA), a region which receives and integrates numerous limbic and non-limbic inputs (e.g., from sensory association cortex, the medial prelimbic and infralimbic prefrontal cortices, and the mediodorsal thalamus). Stimulation within the sensory association cortex, for example, results in strong neuronal excitation within the BLA. If, for example, one were confronted by a growling animal the BLA (via input from the sensory association cortex) may trigger a fear response, signaling the recipient to distance or defend oneself from the potential threat (see Grace, 2003 for review).

The hippocampus, specifically the ventral hippocampus (subicullum), provides input to the NA that is glutametergic in nature. As such, stimulation of the hippocampus produces long (i.e., hundreds of msecs) depolarizations within the NA (O'Donnell & Grace, 1995). These extended depolarizations, in turn, allow for information to flow through to the prefrontal cortex (PFC), after first passing through the ventral pallidum and thalamus. Input from the PFC to the NA results in a hyperpolarization of the BLA via excitation of inhibitory interneurones. Thus, the effect of any stimulatory signals received by the BLA is reduced by this hyperpolarization. In this way, the hippocampus (via limbic-cortical circuitry) acts to gate information from the amygdala (O'Donnell & Grace, 1995). Such input is thought to be involved in context dependency and keeping organisms focused on tasks (Grace, 2003). If, to continue with our example, the animal's growl originated from a small dog secured on its owner's leash, the PFC may override the emotional response (i.e., fear) by evaluating the threat (i.e., the growl) as not harmful (Grace, 2003). Of note, the resulting behavioural output (e.g., petting the dog vs. running from the dog) reinforces a feedback loop through the PFC via the ventral pallidum and mediodorsal thalamic nucleus (Grace, 2000).

Consistent with Grace's (2000) postulation are results from a meta-analytic review of magnetic resonance imaging (MRI) findings in SCZ showing the hippocampus to be the structure with the most volumetric deficiency (Nelson, Saykin, Flashman & Riordan, 1998). Nelson et al.'s (1998) analysis, which included 18 studies, revealed a 4% bilateral reduction in hippocampal volume among individuals with SCZ. Reduced neuronal size and density and increased pyramidal cell disarray within the hippocampus have also been observed in post-mortem examination of individuals with SCZ (Arnold, Franz, Gur, Gur, Shapiro, Moberg, Trohamowski, 1995; Benes, Kwok, Vincent, & Todtenkopf, 1998; Gothelf, Soreni, Nachman, Tyano, Hiss, Reiner, et al., 2000).

Grace has developed a rat model of SCZ whereby administering the mitotoxin, methyl azoxymethanol acetate (MAM) to rats during critical developmental periods (e.g., gestational day 17 [GD17]; Grace & Moore, 1998) he has been able to mimic the cytoarchitectural changes observed in SCZ (i.e., abnormalities in hippocampal, entorhinal cortical, and prefrontal cortical regions; Moore & Grace, 1997). MAM is a DNA methylating agent which arrests cells in the process of division (Cattabeni & Di Luca, 1997). In support of the MAM model's validity as an animal model of SCZ are studies showing that rats treated with MAM show similar behavioural and cognitive abnormalities relative to individuals with SCZ (for review, see Lodge & Grace, 2009). Various investigations using behavioural paradigms such as the pre-pulse inhibition of startle (PPI), latent inhibition, working memory tasks, and hyper-responsivity to psychomotor stimulants, reveal similar behaviours across human SCZ patients and animals treated with MAM (Braff & Geyer, 1990; Flagstad, Glenthoj, & Didriksen, 2005; Goldman-Rakic, 1995; Laruelle, Abi-Dargham, Van Dyck, Gil, D'Souza, Erdo, et al., 1996;

Lubow & Gewirtz, 1995; Moore, Jentsch, Ghajarnia, Geyer, & Grace, 2006; Paulson & Robinson, 1995).

A key element of this model is that onset of MAM-related symptoms are consistent with the developmental course of SCZ – that is, a post-pubertal delay of symptoms. Moreover, behavioural changes are produced only when MAM is administered within a particular developmental window (i.e., GD 17). If, in contrast, MAM is administered on GD15 or earlier, pathological features inconsistent with SCZ develop, including decreases in total cortical mass, microcephaly, and profound cortical dysplasia (Moore et al., 2006).

Lipska's neonatal ventral hippocampal lesion (NVHL) model of schizophrenia. The work of Lipska and colleagues also implicates hippocampal damage in the development of SCZ (see Lipska, Khaing & Weinberger, 1999, for review). To model the cortical pathophysiology of SCZ, these researchers produced excitotoxic lesions of the neonatal rat ventral hippocampus (VH) with the infusion of the ibotenic acid. Animals with NVHLs are observed to share many behavioural phenomena of individuals with SCZ, including hyperlocomotion, excessive reactivity to stress, deficits in social interaction, and deficits in PPI, latent inhibition, as well as an enhanced sensitivity to glutamate antagonists such as MK-801 and PCP (Al-Amin, Weickert, Weinberger, Lipska, 2001; Grecksch, Bernstein, Becker, Hollt, Bogarts & 1999; Le Pen et al., 2000; Lipska & Weinberger, 1993; Lipska & Weinberger, 1994; Lipska, Jaskiw, & Weinberger, 1993). Consistent with the age of SCZ symptom onset among humans, most behavioural alterations observed among NVHL animals appear only after puberty (Lipska & Weinberger, 1998, 2000). Further evidence supporting the validity of the NVHL as an animal model of SCZ comes from the ability of typical and atypical antipsychotic medications to reverse many of the abnormal behavioural and physiological

changes associated with NVHL (Goto & o'Donnell, 2002; LePen & Moreay, 2002; Lipska & Weinberger, 1994).

Research has also shown that the DA mesolimbic-mesocortical systems of NVHL animals are compromised. *In vivo* intracellular recordings of pyramidal neurons in the PFC have revealed an abnormal response to activation of the ventral tegmental area (VTA) in NVHL rats (O'Donnell et al., 2002). Unlike the usual prolonged plateau depolarizing observed with VTA stimulation, abnormal increases in spike firing is observed in NVHL animals. Interestingly, this effect was only observed in animals after puberty (O'Donnell, Lewis, Weinberger, & Lipska, 2002). Similar abnormal responses to VTA stimulation are observed within the NA (Goto & O'Donnell, 2002), and eliminated with PFC lesions (Goto & O'Donnell, 2004). Taken together, these findings have been interpreted as suggesting that disruption of DA activity in the PFC underpins the behavioural abnormalities among NVHL animals, and by extension, those with SCZ (Tseng, Lewis, Lipska, & O'Donnell, 2007).

To understand the delay in symptom onset after the initial lesioning, Lipska and colleagues have also examined disruptions in DA-glutamate interaction, circuitry that continues to mature after puberty (Tseng & O'Donnell, 2005; Tseng et al., 2007). By conducting whole-cell recordings in brain slices obtained from pre- and post-pubertal NVHL animals, Tseng et al. (2007) found that the administration of the D1 agonist (SKF38393) and glutamate agonists (N-methyl d-aspartate [NMDA] and AMPA [α-amino-3hydroxyl-5-methyl-4-isoxazole-propionate]), resulted in increased excitability of deep layer pyramidal neurons in a concentration-dependent manner; however, these findings were only observed in slices from post-pubertal rats, suggesting that PFC DA and glutametergic systems become altered only after puberty in NVHL rats (Tseng et al., 2007).

In summary, the work of Lipska and colleagues strongly implicates neonatal hippocampal damage in the development of SCZ. Moreover, it implicates the hippocampus as playing a causative role in the dopamine and glutametergic dysregulation, including dopamine-glutamate interactions, within SCZ (Lipska et al., 1999; Tseng et al., 2007).

COMT, Schizophrenia, and Cognition. The DTT and DOH have been put forward by Bilder, Volavka, Lachman, & Grace (2004) in order to elucidate tonic/phasic DA dysregulation via Catechol-*O*-methyltransferase (COMT) polymorphisms (Bilder et al., 2004). COMT is an enzyme that catalyses the *O*-methylation of catecholamine neurotransmitters (i.e., alters rate of chemical reaction) such as dopamine, adrenaline, and noradrenalin.[1] Various lines of evidence have motivated the view of COMT as a candidate gene for SCZ. First, as noted above, COMT is involved in the catabolism of DA (Axelrod & Tomchick, 1958), a neurotransmitter system that has been the primary candidate mechanism of SCZ over the past 40-50 years (for review, see Howes & Kapur, 2009). Moreover, researchers have proposed that both SCZ and COMT are associated with cognitive deficits via DA signaling in the PFC (Egan, Goldberg, Kolachana, Coallicott, Mazzanti, Straub, & Goldman, 2001; Goldman-Rakic, 1998; Weinberger, Egan, Bertolino, Callicott, Mattay, Lipska, Berman, & Goldberg, 2001; Bilder,

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[1] The gene that codes for COMT is a functional single nucleotide polymorphyism (SNP) located on the long arm of chromosome 22, initially described by Axelrod & Tomchick (1958). The COMT SNP involves a guanine (G) to adenine (A) transition at codon 158 of the COMT gene, resulting in a valine (val) to methionine (met) substitution. The val allele codes for a high-activity isoform of COMT that rapidly catabolizes dopamine (DA) while the met allele encodes a low-activity isoform of COMT (Axelrod & Tomchick, 1958). The differential rates in DA catabolism associated with COMT bi-allelic variation results in a three- to four-fold reduction in COMT activity among Met homozygotes, relative to Val homozygotes, with heterozygotes demonstrating intermediate activity (Weinshilboum, Otterness, Szumlanski, 1999). It is primarily expressed in its membrane-bound (MB-COMT) form in postsynaptic neurons (Matsumoto, Weickert, Akil, Lipska, Hyude, Herman, et al., 2003). COMT-knockout mice have been found to show marked increases in prefrontal dopamine pools (Gogos, Morgan, Luine, Santha, Ogawa, Pfaff, & Karayiorgou (1998). COMT has a relatively greater influence, via dopamine catabolism, within cortical rather than subcortical areas, presumably due to the relative lack of DA transporters (DAT) within synapses in this region (Lewis et al., 2001). In contrast, within brain regions such as the striatum where other, more efficient, routes of elimination are available (e.g., dopamine transporters [DAT], monoamine oxidease [MAO]), COMT is less available for catabolism via COMT.

Volavka, Czobor, Malhotra, Kennedy, Goldman, Hoptman, et al., 2002; Goldberg et al., 2003; Han, Kee, Min, Lee, Na, Park, & Lyoo, 2006). Accordingly, numerous studies have investigated a genetic linkage between the COMT polymorphism and SCZ; however, their findings have been inconsistent (for review, see Glatt, Faraone, & Tsuang, 2003). Some studies find preferential transmission of the high activity val allele to SCZ offspring (Egan et al., 2001; Li, Sham, Vallada, Xie, Tang, Liu, & Collier, 1996; Kunugi, Vallada, Curtis, Sham, Hoda, Arranz, Nanko, et al., 1997; Li, Ball, Zhao, Murray, Liu, Shan, & Collier, 2000), while others found no association with the illness (Karayiorgou, Gogos, Galke, Wolyniec, Hestadt, Antonarakis, Kazazian, et al., 1998; Strous, Bark, Woerner, Lachman, 1997; Wei & Hemmings, 1999).

Despite the variability in association between the COMT polymorphism and SCZ, examining the relationship between levels of SCZ symptomatology and the COMT polymorphism has revealed interesting findings. Among individuals with SCZ, for example, the val allele is associated with more positive symptomatology than is the met allele (Goghari & Sponheim, 2007). Among healthy subjects, Avramopoulos, Stafanis, Hantoumi, Smyrnis, Evdokimidis, & Stefanis (2000) found that males expressing the val/val bi-allelic variation of COMT had the highest levels of schizotypy. When examining COMT-personality interactions among HCs, Sheldrich, Krug, Markov, Leube, Michel, Zerres, Eggermann, & Kircher (2008) revealed an association between the val allele and higher scores on scales measuring disorganized behavior and speech among persons with Schizotypal Personality Disorder (SPD).

With regard to cognition, the val allele has been found to be associated with poorer performance on prefrontally-mediated cognitive tasks among individuals with SCZ and SPD, including executive functioning, processing speed, and attention (Egan, et al., 2001; Weinberger,

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Egan, Bertolino, et al., 2001; Bilder, et al., 2002; Goldberg et al., 2003; Han et al., 2006; Minzenberg, Xu, Mitropoulou, et al., 2006). COMT genotypes have also been shown to interact with cognitive functioning in a similar fashion among healthy controls (HCs). The expression of the met allele among HCs, for example, is associated with significantly fewer perseverative errors on the WCST (Malhotra, Kestler, Mazzanti, Bates, Goldberg, & Goldman, 2002) while individuals with the met/met genotype perform better on Trail Making Test-B (Sheldrich et al., 2008), tests of executive functioning, and visuospatial tasks (Bruder, Leo, J.G., Xu, H., 2005; de Frias, Annerbrink, Westberg, Eriksson, Adolfsson, & Nilsson, 2005). The val allele has also been implicated in impaired cognitive performance within animal models of the COMT polymorphism. Specifically, transgenic mice engineered to over-express a human COMT val polymorphism (Val-tg) show disrupted attentional set-shifting abilities and impaired working memory and recognition memory. Despite various studies showing a significant relationship between COMT and cognition, others fail to do so (Stefanis et al., Tsai, Yu, Chen, Chen, Liou, Chen, & Hong, 2003).

Recently, Bilder et al. (2004) proposed that such variability may be due, in part, to the differential effect of the *Comt* val[158]met alleles on different types of cognitive tasks. They purport that the val allele, which codes for a high activity isotope of COMT, facilitates switching or transitioning to alternate network states mediating the resetting of behavioural programs (i.e., facilitation of the ventral trend) (Bilder et al., 2004). The met allele, in contrast, is associated with low activity COMT and regulates goal directed activity (i.e., facilitation of the dorsal trend) (for review, see Bilder et al. 2004). Given that the high-activity form of COMT (i.e., the val allele) leads to cortical hypodopaminergia, thereby increasing the risk of SCZ (Egan et al., 2001),

this model suggests that genetics may mediate the preferential dorsal trend impairment among individuals with SCZ.

The majority of studies examining the effect of COMT genotype on cognitive functioning have not specifically addressed Bilder et al.'s (2004) model, owing, in part, to the fact that most cognitive paradigms used to examine COMT effects are complex and require both switching to alternate network states (i.e., cognitive flexibility) and the maintenance of behavioural programming (i.e., cognitive stability). However, the Competing Paradigm Task independently assesses cognitive stability and cognitive flexibility (Nolan, Bilder, Lachman, & Volavka, 2004). In the Competing Paradigm Task participants are presented with one or two cues and asked to follow one or two alternating rules (e.g., press a key the same number of times as there were cues [imitation] or press once for two cues and twice for one cue [reversal]). When examining the performance of SCZ patients on the Competing Paradigms Task, Nolan et al. (2004) found that met homozygotes had better acquisition of the imitation rule, but greater deficit shifting from imitation to reversal, relative to val homozygotes. Thus, an increase in tonic DA appears to confer an advantage on tasks requiring cognitive stability (imitation task) while also conferring a disadvantage on a task requiring cognitive flexibility (reversal task). Notably, an index of 'switch cost' (i.e., the cost of switching tasks, controlling for overall performance), shared 42% variance with genotype, suggesting COMT plays a central role in cognitive tasks requiring cognitive stability and flexibility via prefrontal dopamine regulation.

Visual system evidence of dorsal trend deficits in SCZ

A large literature suggesting dorsal trend impairment in SCZ derives from investigations of the visual system, in particular studies interrogating the integrity of the two major visual systems delineated within the dual processing model of vision (DPM) (Goodale &

Milner, 1992; Mishkin, 1966; Ungerleider & Mishkin, 1982). The DPM specifies two separate visual pathways in the brain, which are consistent with the DTT (Pandya et al., 1988). The ventral stream projects largely from parvocellular cells within the striate cortex to the inferotemporal cortex and is responsible for the perceptual identification of objects. In contrast, the dorsal stream, which projects largely from magnocellular cells within the striate cortex to the posterior parietal regions, subserves spatial cognition and the required sensorimotor transformations of visually guided actions (Goodale & Milner, 1992). The DPM has been widely supported by anatomic (Mishkin, 1966, 1972; Ungerleider & Mishkin, 1982), physiological (Desimone & Ungerleider, 1989; Van Essen & Maunsell, 1983), and neuroimaging (Haxby, Grady, Horwitz, Ungerleider, Mishkin, Carson, Herscovitch, et al., 1991; Haxby, Horwitz, Ungerleider, Maisog, Pietrini, Grady, 1994; Horwitz, Grady, Haxby, Schapiro, Rapoport, Ungerleider, & Mishkin, 1992; McIntosh, Grady, Ungerleider, Haxby, Rapoport, & Horwitz, 1994) research.

When the visual system in persons with SCZ has been evaluated, results point to disproportionate impairment of the dorsal visual pathway. Individuals with SCZ, for example, show marked deficits in behavioural tasks highly dependent on magnocellular input to the dorsal visual stream, such as motion detection and backward masking (Cadenhead, Serper, & Braff, 1998; Chen, Nakayama, Levy, Matthysse & Holzman, 2003; Chen, Palafox, Nakayama, Levy, Matthysse, & Holzman, 1999; Green, Mintz, Salveson, Neuchterlein, Breitmeyer, Light, Craft, 2003; Li, 2002 Schechter, Butler, Sillip, Zemon & Javitt, 2003). Other functions known to be dorsally-mediated, such as susceptibility to visual illusions in grasping behaviour have also been found to be impaired among individuals with SCZ (King, Christensen & Westwood, 2008).

Neuroimaging investigations of visual processing have also shown dorsal impairment among individuals with SCZ (Braus, Weber-Fahr, Tost, Ruf, & Henn, 2002); Butler, Schechter, Zemon, Schwartz, Greenstein, Gordon, et al., 2001; Butler, Zemon, Schechter, Saperstein, Hoptman, Lim, Revheim, et al., 2005; Butler, Martinez, Foce, Kin, Zemon, Silipo, & Javitt, 2007). Using functional magnetic resonance imaging (fMRI), for example, Braus et al. (2002) found dorsal impairment during a task requiring attention to the simultaneous presentation of a moving 6-Hz checkerboard and an acoustic stimulus (i.e., drumbeats). Individuals with SCZ demonstrated reduced activation in the right thalamus, right PCF (i.e., at the level of frontal eyefields and Brodmann Area [BA] 46), and bilateral parietal lobes restricted to the dorsal visual pathway. Convergent findings have also been observed when employing EEG to identify neural correlates of viewing stimuli designed to bias the visual system toward either magnocellular (i.e., dorsal) or parvocellular (i.e., ventral) stimuli (Butler et al., 2001; Butler et al., 2007). In these experiments, Butler et al. (2001, 2005, 2007) found that the signal-to-noise ratios for visual evoked response potentials (ERPs) were significantly lower for individuals with SCZ compared to controls in conditions that biased processing towards the magnocellular (dorsal) pathway (e.g., stimuli of low-contrast). In more recent investigations Butler and colleagues have shown, through diffusion tensor imaging (DTI), that decreased magnocellular-biased visual ERPs correlate with decreased white matter integrity in the optic radiations, which project from LGN to striate cortex. Of note, decreased magnocellullar-biased visual ERPs were also found to negatively correlate with indices of goal-directed, volitional behaviours (i.e., dorsally-mediated), including working memory, global intellectual functioning, and aspects of functional outcome (Butler et al., 2005).

Deficits in cognitive control suggest dorsal trend impairment in SCZ

Further support for disproportionate impairment in the dorsal trend comes from the investigation of cognitive control within SCZ. Cognitive control (CC) has been defined as the capacity to flexibly direct resources to a goal by selecting and integrating relevant contextual information and has been widely examined by Cohen and colleagues (Barch, Braver, Akbudak, Conturo, Ollinger, & Snyder, 2001; Braver, Barch, & Cohen, 1999; Braver & Cohen, 1999; Cohen, Braver, & O'Reilly, 1996; Cohen & Servan-Schreiber, 1992; for review, Barch & Braver, 2005). Of relevance, is the finding that SCZ-related impairments in CC appear to be mediated by DLPFC dysfunction (Barch et al., 2001; Cohen & Servan-Screiber, 1992). Cohen and colleagues postulate that the failures of CC observed among persons with SCZ are due to a fundamental impairment in their ability to internally represent, maintain, and update context information. Moreover, they have proposed that a deficit in the processing of context information underlies related cognitive deficits such as disturbances in attention, working memory, and inhibition (Barch et al., 2001; Braver, Barch, & Cohen, 1999; Braver & Cohen, 1999; Cohen, Barch, Carter, & Servan-Schreiber, 1999; Cohen & Servan-Screiber, 1992). This model does not involve dedicated 'inhibitory' or 'working memory' mechanisms; instead, deficits in context representation are theorized to achieve the same behavioural outcome by a failure to provide top-down support for task-relevant processes. Within both types of tasks, context representations serve an attentional function through biasing the selection of task-relevant information over other potentially competing sources of information. Context representations can include task instructions, a specific prior stimulus, or the result of processing a sequence of prior stimuli (Barch, Mitropoulou, Harvey, New, Silverman, & Siever, 2004).

In order to explicitly measure context processing in individuals with SCZ, a modified Continuous Performance Task (CPT), referred to as the AX-CPT, has been employed (Cohen et al., 1999; Servan-Schreiber, Cohen, & Steingard, 1996). In this task participants are presented with cue-probe pairs and instructed to make a target response to an "X" (probe) but only if it follows an "A" (cue). Seventy percent of trials are AX pairings, while 30% are distributed across three types of nontarget trials: BX, AY, BY, with "B" representing non-A cues and Y representing non-X probes. Under these task constraints, two types of biases are created. First, a bias towards the prepotent response – i.e., participants will expect to make a target response when they see an "X" probe, because this is the correct response on most of the trials (i.e., 87.5% of the trials in which an X is presented). On "BX" trials participants must use the context provided by the "B" cue to inhibit this prepotent response. Thus, impaired context representations will lead to poor performance on "BX" trials, because context provided by the "B" cue would not be available to the participant to override the tendency to respond to the target, "X".

The second bias is that participants expect to make a target response after they see an "A" cue, because most of the time an "X" follows the "A" cue (87.5% of the "A" cue trials). However, on trials in which the "A" is not followed by an "X", this predictive aspect of context actually creates the tendency to respond (i.e., to make a false alarm). Thus, intact representations of context will hinder performance on "AY" trials, because context induces an invalid expectancy, leading to worse "AY" than "BX" performance. Accordingly, individuals with impaired context representations should show worse "BX" than "AY" performance.

The AX-CPT involves an additional manipulation; specifically, it allows for the examination of context maintenance by manipulating the delay (i.e., the stimulus-onset

asynchrony [SOA]) between the cue and probe, thereby increasing the degree to which context must be actively maintained in working memory. According to the assertions of this model, when context is maintained, then the strength of context representations should stay the same or increase with delay (Braver et al., 1999; Braver, Cohen, & Servan-Schreiber, 1995). Intact maintenance should translate into the same or improved performance on "BX" trials because there is greater opportunity for context information to inhibit an incorrect response to the "X". In contrast, the model predicts that greater delay within "AY" trials will translate into more opportunity for context representations to induce the participant to prepare for a target response, which must be inhibited when a "Y" rather than an "X" occurs.

Consistent with the proposition that individuals with SCZ have impaired context processing is the finding that they make greater "BX" errors, including increased RTs on these trials, but significantly fewer "AY" errors, particularly at the longer delay (Barch et al., 2001). These findings suggest that context representations are less available, or at least less able to influence processing, among patients with SCZ. The same impairment in processing context information has also been found to result in the less predictive use of context (i.e., the "A") on "AY" trials, which among HCs typically leads to relatively greater errors on "AY" trials. Interestingly, individuals with SCZ were not significantly slower than controls on "AY" trials, suggesting that they actually experience less context-induced interference (Barch et al., 2001).

Evidence supporting a deficit among SCZ patients in context maintenance (vs. context representation) has been less than straight-forward. For example, some studies have found SCZ participants to have increases in context processing deficits at the long compared to short delays (Cohen et al., 1999; Elvevag, Duncan, & McKenna, 2000; Javitt, Shelley, Silipo, & Lieverman, 2000; Servan-Screiber et al., 1996; Stratta et al., 1998; Stratta et al., 2000) while others have not

(Barch et al., 2001; Barch, Carter, MacDonald, Braver, & Cohen, 2003; Perlstein, Diit, Carter, Noll, & Cohen, 2003). Barch & Braver (2005) provide two potential explanations for these contradictory findings. First, they suggest that discrepancies may reflect the chronicity of illness among study participants. Specifically, SCZ participants early in the course of their illness have not demonstrated increases in "BX" errors at the long (vs. short) delays, or show smaller increases relative to chronic SCZ patients. Indeed, they have greater "BX" error rates and RTs at long (vs. short) delays. Second, among studies using chronic SCZ patients, the HCs also display increases in BX errors or RTs from the short to long delay, making it difficult to detect differentially greater deficits in context processing in patients (Barch & Braver, 2005).

Central to Cohen and colleagues' theory of context processing is the assertion that impairment in the internal representation, maintenance, and updating of context information is due to dopamine dysregulation which, in turn, leads to abnormal gating of information into the PFC. Consistent with the DTT, they hypothesize that the DLPFC, in particular, mediates the processing of context (Barch et al., 2001; Cohen & Servan-Screiber, 1992). In addition to the various lines of evidence suggesting structural and functional damage to the DLPFC (reviewed above), Cohen and colleagues have employed computational modeling as a means of explicitly specifying and examining the neural mechanisms supporting context processing (e.g., functioning of DLPFC and DA system) (Braver, 1997; Braver et al., 1999; Braver, Barch, & Cohen, 1999; Braver, Cohen, & Servan-Screiber, 1995; Cohen & Servan-Schreiber, 1992). Overall, their simulation results are consistent with impairments in context processing that are mediated by impairments in abnormal dopamine activity within the PFC.

Relative sparing of the ventral pathway in schizophrenia

In contrast to the above-reviewed evidence for dorsal trend dysfunction, research has found evidence for a relative sparing of ventral trend functioning among individuals with SCZ (Braus et al., 2002; Butler et al., 2001; Butler et al., 2007). For example, although Braus et al. (2002) found SCZ patients to have reduced signal-to-noise ratios for visual ERPs in conditions that bias processing towards the magnocellular (dorsal) pathway, no activation differences in the primary visual cortex (V1) or in occipitotemporal (ventral) pathways were observed. That these findings were observed among neuroleptic naïve patients argues that this dissociation is a result of the SCZ *per se* and not secondary to pharmacological treatment. Similarly, Butler et al. (2001, 2005, & 2007) found that the signal to noise ratios for visual ERPs for individuals with SCZ were significantly lower compared to controls in conditions that biased processing towards the magnocellular pathway but not in the conditions biased toward the parvocellular pathways.

Intact functioning has also been observed on other ventrally-mediated tasks such as the Iowa gambling task (IGT), a test of probabilistic intuitive reasoning (Bechara, Damasio, Damosio, & Anderson, 1994; Wilder, Weinberger, Goldberg, 1998). The IGT is routinely used to infer functioning within the orbital frontal cortex (OFC). In the IGT participants must choose among decks of cards which yield high immediate gain but larger future loss and decks which yield lower immediate gain but a smaller future loss. Wilder et al. (1998) found that individuals with SCZ performed similar to controls on the IGT. Importantly, Wilder et al. (1998) did not find that performance on the IGT was correlated with dorsally-mediated cognitive functions such as working memory. This finding has since been replicated by independent researchers among stabilized first-episode as well as more chronically medicated patients with SCZ (Cavallaro,

Cavedini, Mistretta, Bassi, Angelone, Ubbiali & Bellodi, 2003; Rodriguez-Sanchez, Crespo-

Facorro, Iglesias, Gonzalez-Blanch, Alvarez, Llorca, & Vazquez-Barquero, 2005). Intact

performance on the IGT by SCZ patients has been observed within the context of impaired

DLPFC functioning, as indexed by performance on the WAIS-III digits backwards, verbal

fluency (FAS), Trail Making Test, and the Wisconsin Card Sorting Test (WCST; Cavallaro et al.,

2003; Rodriguez-Sanchez et al., 2005). Cavallaro et al.'s (2003) study design was particularly

elegant in that it allowed for the examination of a double dissociation of frontally-mediated

functions between individuals with SCZ and those with obsessive-compulsive disorder (OCD), a

population with known orbitofrontal dysfunction. This study revealed that SCZ patients

performed significantly worse than OCD patients on the WCST, while OCD patients performed

significantly worse than SCZ subjects on the IGT.

Additional support for a relative ventral trend sparing in individuals with SCZ can be

found in the work of Abruzzese and colleagues who have used the object alternation task (OAT)

to show intact orbitofrontal functioning within this population (Abruzzese, Ferri, Bellodi, &

Scarone, 1995; Abruzzese, Ferri & Scardone, 1997). In the OAT, participants are required to

retrieve an object (e.g., penny) hidden under one of 2 plaques placed in front of them. After a

correct response the administrator hides the penny under the opposite plaque. Originally

developed to measure orbitofrontal functioning in nonhuman primates (Mishkin, 1964; Mishkin,

Vest, Waxler & Rosoldk, 1969), the OAT has been adapted by Freedman and colleagues (1986a,

1986b, 1990) to index OFC functioning among humans. Abruzzese et al. (1995, 1997) found

that individuals with SCZ have intact performance on the OAT. Moreover, when comparing

performance on the OAT with that of the WCST across individuals with SCZ and those with

OCD, Abruzzese et al. (1995, 1997) demonstrated a similar double dissociation to that observed

by Carvallo et al. (2003), whereby individuals with SCZ perform worse than individuals with OCD on the WCST but better on the OAT. Importantly, this functional double dissociation is thought to reflect the neuroanatomical double dissociation with SCZ being preferentially affected by DLPFC damage and OCD preferentially impacted by OFC damage (Abruzzese et al., 1995, Abruzzese et al., 1997).

To summarize, studies of brain morphology, regional brain blood flow, and cognition suggest that SCZ may be preferentially associated with dorsal trend impairment in the context of relative ventral trend sparing (Abruzzese et al., 1995; Abruzzese et al., 1997; Butler et al., 2001; Butler et al., 2005; Butler et al., 2007; Cavallaro et al., 2003; King et al., 2008; O'Donnell et al., 2002). Importantly, however, while the DTT has been helpful in understanding the cognitive strengths and weaknesses of persons with SCZ, a persistent inconsistency exists; namely, that action inhibition (AI), a well-accepted ventrally-mediated function, is generally observed to be impaired among this patient population (Badcock, Michie, Johnson, Combrinck, 2002; Bellgrove, Chambers, Vance, Hall, Karamitsios, & Bradshaw, 2006; Gooding, Kwapil, Tallent, 1999; Kiehl, Smith, Hare, & Liddle, 2000; Rubia, Russel, Overmeyer, Brammer, Bullmore, Sharma, Simmons, et al., 2001; Weisbrod, Kiefer, Marzinzik & Spitzer, 1999). Explanations for this inconsistency are the focus of the current thesis. In the following sections I will introduce the neurobiology and experimental phenomenology of AI before explicating the specific hypotheses and methods of the experiments comprising this thesis.

Action inhibition: a ventrally-mediated function

AI refers to the ability to prevent any form of planned physical response (Eagle, Bari, & Robbins, 2008). The construct is commonly and interchangeably referred to as response inhibition. For the sake of continuity, however, this construct will be labeled as AI throughout

the present document. Substantial empirical evidence suggests that AI is a function of the PFC

(Aron, Fletcher, Bullmore, Sahakian & Robbins, 2003). However, until recently its exact

localization was difficult to ascertain as many of the early studies supporting this contention

commonly involved individuals with large, non-discrete lesions in the frontal lobe (for review,

see Aron et al., 2003). More recently, functional neuroimaging has localized AI to the inferior

frontal gyrus (IFG), specifically the right IFG, among healthy volunteers (Aron et al., 2003;

Aron, Robbins, Poldrack, 2004; Aron & Poldrack, 2006; Aron, Behrens, Smith, Frank, &

Poldrack, 2007; Chambers, Bellgrove, & Sokes, 2006; Chevriet, Noseworthy, Schachar, 2007;

Forstmann Wildenberg, & Ridderinkhoff, 2008; Konishi, Nakahima, Uchida, Sekihara, &

Miyashita, 1998, Konishi, Nakahima, Uchida, Kikyo, Kamayana, & Miyashita, 1999; Pliszka,

Glahn, Semrud-Clikeman, Kranklin, Perez, Xiong, & Liotti, 2006; Rubia, Russel, Bullmore,

Soni, Brammer, Simmons, Taylor, et al., 2001b, Rubia, 2003). This finding seems consistent

across various paradigms of AI, including the Stop-Signal paradigm (SSP), Go/NoGo tasks, and

the Flanker task. Moreover, Forstmann et al. (2008) have shown that activation in the right IFC

covaries with the reaction time distribution measure of AI (i.e., the Stop-Signal Reaction Time

[SSRT]), further arguing for its contributing role in AI. More recent work using diffusion tensor

imaging has implicated a more extensive inhibitory neuroanatomical network. Aron et al. (2007)

correlated individual brain activation from regions of interest with the individual SSRT and

delineated a densely inter-connected network consisting of the right IFG, the right pre-

supplementary motor area, and the subthalamic nucleus.   Activation within this network was

shown to covary with individual differences in AI as measured by SSRT (Aron et al., 2006; Aron

et al., 2007).

Additionally, individuals with OFC damage also show AI deficits (Rieger, Gauggel, Burmeister, 2003). Among nonhuman primates, lesions within the VLPFC results in greater errors on NoGo trials of the Go/NoGo task, in the absence of differences in overall error rates (i.e., error rates amalgamating impaired performance across Go and NoGo trials; Iversen & Mishkin, 1970). Similarly, lesions within the VLPFC of marmoset monkeys have been shown to result in difficulty shifting between successive sorting rules on the WCST (i.e., difficulty inhibiting their prepotent response to previously reinforced sorting category; Dias, Robbins & Roberts, 1997). Investigations using single cell recordings of monkeys executing a Go/NoGo task also implicate ventral structures in the mediation of AI (Sakagami & Tsutsui, 1999). Specifically, neurons within the VLPFC show greater activation immediately after receiving the NoGo signal and before response execution yet show no motor response related activity at the time of response execution.

Interestingly, Sakagami, Xiaochuan & Uttl (2006) have recently formulated a decision-making theory in which they propose that AI serves a critical role in ones' ability to make appropriate decisions, including action plans. Notably, their theory is couched within a dual pathways framework, consistent in both structure and function, with the DTT, the DOH, and the DPM. Sakagami et al. (2006) construe these pathways as extensions of the dorsal and ventral visual pathways initially articulated by Ungerleider & Mishkin (1982) and later elaborated by Goodale & Milner (1992), and are thus labeled the extended dorsal (E-dorsal) and extended ventral (E-ventral) pathways. Of particular relevance to the current discussion is Sakagami et al.'s contention that AI is mediated by the E-ventral pathway, specifically the VLPFC.

Despite research findings suggesting relative sparing of ventrally-mediated functions among individuals with SCZ, AI deficits are frequently observed (Badcock et al., 2002; Gooding

et al., 1999; Kiehl et al., 2000; Rubia et al. 2001). Such impairment is observed across a number

of tasks thought to gauge AI. On the WCST, for example, individuals with SCZ routinely

perseverate, which is commonly interpreted as a failure to inhibit ones' prepotent response to

previously reinforced sorting rules (Gooding et al., 1999; for review see Laws, 1999). Deficits

are also observed when employing tasks considered purer measures of motor AI, such as the SSP

(Badcock et al., 2002) and Go/NoGo tasks (Kiehl et al., 2000; Rubia et al. 2001).[2]

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[2] Although Go/NoGo tasks typically assess AI using visual cues as the imperative stimuli, impaired AI has also been observed when employing tasks requiring the processing of auditory Go and NoGo signals (Weisbrod, Kiefer, Marzinzik & Spitzer, 1999).

Proposed explanation for AI deficits in SCZ

Despite findings of impaired AI among individuals with SCZ, the current thesis raises the possibility that SCZ may not cause AI deficits *per se*. Instead, we propose that there are problems inherent among measures used to gauge AI in SCZ – namely, that paradigms purporting to measure AI deficits routinely conflate AI with other cognitive operations. For example, in addition to requiring participants to inhibit a prepotent response (e.g., to the Go signal), the Go/NoGo task also requires intact working memory, visual perception, and the representation and maintenance of context information. Thus, on AI tasks, in addition to being able to inhibit their prepotent responses, participants must also be able to accurately detect and interpret the stimuli which signal them to inhibit their response. The degradation or interference of this signal can presumably result in performance decrements. For example, if stimuli are presented for shorter periods or the stimuli share more similar perceptual characteristics (i.e., decreasing the distinctiveness of the Go versus NoGo signals) accurate processing of the stimuli will be compromised and the manifest behavioural output more error ridden.

Given that individuals with SCZ routinely show impairment across a wide range of cognitive functions, it is unclear whether impairment on AI tasks is due solely to an inhibitory deficit or other requisite cognitive operations. In fact, various lines of evidence suggest that individuals with SCZ have particular difficulty interpreting the meaning, and inferred action, of task stimuli on tests of AI (Honey, Pomarol-Clote, Corlett, Honey, McKenna, Bullmore & Fletcher, 2005; Nuechterlein, 1983b). Within the degraded CPT, for example, persons with SCZ show disproportionately greater inhibitory error rates, presumably because of a disproportionate difficulty deciphering task stimuli. Thus, behavioural deficits are thought to result directly from

their inability to accurately interpret the meaning of task stimuli and/or transmit perceptual information to valid action patterns. Within the context of the DTT, the maintenance of veridical perceptual representations (i.e., context) and the coupling of these to goal-directed action is the territory of the dorsal trend. It follows, therefore, that deficits in these operations could unduly impact performance on tasks whose output depend on them – for example, conventional AI tasks. It is the contention of the current thesis, therefore, that previous data showing impaired AI were plausibly generated by deficits across factors that increase the difficulty of deciphering, interpreting, maintaining, or utilizing task stimuli, which would ultimately interfere with speeded and/or accurate responses and yet remain separable from inhibition *per se*. In this context, deficits among SCZ participants on conventional AI tasks could be secondary to impairments governed by dorsal trend dysfunction and, therefore, do not necessarily implicate dysfunction in ventral trend structures.

Task complexity as a confound in AI tasks

A recent meta-regression analysis has questioned the validity of the SSP in independently assessing inhibitory deficits (Huizenga, van Bers, Plat, van den Wildenberg, & Molen, 2009). Specifically, Huizenga et al. (2009) analyzed 41 studies involving the stop signal performance of children with ADHD, examining the impact of task complexity on AI deficits. Two indices of task complexity were used: mean reaction time to the Go signal and the spatial compatibility of the stimulus-response mapping in the Go task. An example of a spatially compatible task involved the participant moving a computer mouse toward the target stimulus on the computer screen. An example of a spatially incompatible task required the translation of a non-spatial stimulus (e.g., X and O) into a spatial response (e.g., pressing one of two keys). Increased group differences (i.e., ADHD vs. controls) in SSRTs were associated with increased task complexity,

as indexed by Go reaction time. It was also found that large SSRT differences were associated

with spatially non-compatible responses, whereas small SSRT differences were associated with

spatially compatible responses. These results suggest that the magnitude of SSP inhibitory

deficits depends on the complexity of the Go task (Huizenga et al., 2009). In addition, if

performance on the SSP in individuals with marked inhibitory deficits (i.e., children with

ADHD) is confounded by task complexity, it seems reasonable that the performance of

individuals from other clinical populations (e.g., SCZ) may also be similarly confounded.

Using a flanker task, Takezawa & Miyatani (2005) also found that complexity impacted

the rate of inhibitory errors. Specifically, in addition to manipulating the congruency of stimuli

(e.g., directions of target and distracters), Takezawa & Miyatani (2005) manipulated conflict by

varying the distance between the target and directional distracters. In addition to finding an

effect of congruency (i.e., longer RTs on incongruent trials), they also found an effect of conflict.

That is, within congruent trials, RTs increased as the amount of conflict in the preceding trial

increased (Takezawa & Miyatani, 2005). These results suggest that response conflict (CON) can

result in behavioural adjustments (e.g., increases in RTs), even in congruent conditions.

The impact of manipulating stimulus discriminability on individuals with SCZ

Indeed, there appears to be support for the notion that individuals with SCZ show

disproportionately high inhibitory errors in response to increased task complexity (Nuechterlein,

1983b). For example, individuals with SCZ, or those at-risk of developing SCZ, show

disproportionately high inhibitory errors when task stimuli are visually obscured, thus decreasing

their discriminability and/or decipherability. Although task complexity can be manipulated in a

variety of ways, the current discussion will focus on studies in which complexity has been

operationalized as the discriminability of task stimuli. For example, although individuals at risk

for developing SCZ show very low levels of errors on a traditional CPT task (Nuechterlein, 1983a), increased error rates are observed on versions in which task stimuli were degraded (Nuechterlein, 1983b). Tasks such as the CPT, and other typical simultaneous-discrimination tasks, entail an encoding of stimulus patterns to the recognition level that may either occur "automatically" or with only limited demands on processing capacity (Posner, 1978; Shiffrin & Schneider, 1977). By degrading CPT stimuli, Nuechterlein (1983b) found that HCs show impaired signal detection, which translates into higher error rates. Stimuli were degraded at three levels – low, moderate, and high blurring or defocusing of the image. Children of mothers with SCZ were disproportionately impacted by stimulus degradation in relation to children of mothers with nonpsychotic psychiatric disorders, as well as hyperactive children. These findings suggest that AI performance is directly impacted by manipulations of stimulus decipherability among persons with SCZ-spectrum disorders.

Disentangling neuroanatomical substrates of AI and task complexity

Importantly, preliminary findings suggest that the behavioural dissociation of inhibitory demands from task complexity is also reflected in the underlying neuroanatomy thought to mediate these processes. Although the IFG is most commonly implicated in the mediation of AI, theoretical claims and empirical findings exist to support dorsal mediation of cognitive processes needed to contend with task complexity (Botvinick, 2007; Durston et al., 2002; Nee, Wager, & Jonides, 2007). The DLPFC, for instance, is often activated during conventional tasks of AI (Perlstein et al., 2003; de Zubicaray, Andrew, Zelaya, Williams, & Dumanoir, 2000; MacDonald, Cohen, Stenger, & Carter, 2000; McDowell et al., 2002; Nee et al., 2007; Durston et al. 2002). The DLPFC is thought to underpin the representation and maintenance of context information over time, processes important in using inhibitory signals to guide movement appropriately

(Barch, Braver, Nystrom, Forman, Noll, & Cohen, 1997; Braver & Cohen, 2001). We view

these tasks as relying more on ones' ability to decipher the meaning of task stimuli, in the

context of closely presented stimuli, rather than relying on AI *per se*. The ACC is regularly

activated during tasks of AI (Carter et al., 2001; Honey et al., 2005; Kok, 1986; Braver, Barch,

Gray, Molfese, & Snyder, 2001; de Zubicaray et al., 2000; Durston et al., 2002). In addition,

activation within the ACC appears to be particularly sensitive to manipulations in the

decipherability of inhibitory stimuli. For example, when using a modified Go/NoGo task in

which the visual discriminability of Go and NoGo signals were altered, Kok (1986) found

reduced activation over scalp areas indicative of ACC functioning. Within this paradigm,

discriminability was manipulated by superimposing a grid containing 81 (9x9) dots onto the

stimuli (i.e., letters A, B, or C). Kok's (1986) findings suggest that the ACC plays a particularly

important role in interpreting meaning of the imperative stimulus in Go/NoGo tasks.

Within tasks of AI, we contend that discriminating and deciphering task stimuli directly

impacts ones' ability to resolve conflict between potential, yet opposing, behavioural responses

(e.g., CON between Go and NoGo stimuli). Thus, the greater the similarity between these

stimuli, the greater the CON. Importantly, CON has also been parametrically achieved through

other means. Kerns, Cohen, MacDonald, Cho, Stenger, Aizenstein, & Carter (2004), for

example, used the Stroop Colour-Naming Test (Stroop) to increase CON. Within the Stroop,

conflict occurs when the accurate response (i.e., naming the colour in which the word is printed)

conflicts with the participants' prepotent response (i.e., to read the printed word). Using

functional magnetic resonance imaging (fMRI), Kerns et al. (2004) demonstrated increased ACC

activation on trials involving conflict. Moreover, CON-related ACC activation predicted greater

DLPFC activation (i.e., right middle frontal gyrus, BA9, 8; right superior frontal gyrus, BA9, 10)

on subsequent trials, suggesting the influence of ACC activation on DLPFC activity. ACC

activation in such trials also predicted adjustments in behaviour on the trials directly following

conflict trials. That is, RTs were found to be slower on congruent trials preceded by incongruent

trials versus congruent trials that were preceded by congruent trials. These results are consistent

with the Conflict Monitoring hypothesis, which postulates that the monitoring of CON, achieved

by the ACC, acts to signal other brain structures (e.g., PFC) to engage CC (Botvinick, Braver,

Barch, Carter & Cohen, 2001). These findings also represent direct evidence that CON-related

activity in the ACC predicts a subsequent increase in PFC activity and that the occurrence of

CON (and the subsequent engagement of CC) results in behavioral adjustments (Botvinick et al.,

2001). Kerns et al.'s (2004) findings provide evidence that the ACC is co-activated with other

cortical regions during AI and that such activation is associated with compensatory behavioural

strategies.

   Impaired ACC functioning during AI tasks in SCZ. A number of investigators have

shown reduced ACC activation among individuals with SCZ during tasks of AI. Using fMRI,

Laurens, Ngan, Bates, Kiehl, & Liddle (2003) found decreased rostral ACC activation among

individuals with SCZ during errors of commission while completing the Go/NoGo task. In

contrast, HCs were found to recruit the rostral ACC during errors of commission (Laurens et al.,

2003). This finding suggests that CON is registered within the ACC among HCs but not among

individuals with SCZ. Consistent with these findings are results from an fMRI study conducted

by Rubia et al. (2002) in which decreased activation within the ACC was observed among SCZ

participants during the SSP. Event-related potential (ERP) investigations have shown similar

findings. For instance, Kiel et al. (2000) found that individuals with SCZ, relative to HCs, failed

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to show larger N275 in the mid frontal region on NoGo relative to Go trials. N275 in this region is thought to be a marker of ACC functioning (Kiel et al., 2000).

Paradigms implementing discriminability manipulations have shown that individuals with SCZ have disproportionately reduced ACC activation as task stimuli become less easily decipherable – that is, when CON is increased. For instance, reduced hemodynamic activity within the caudal ACC was observed in SCZ by Carter, MacDonal, Ross, & Stenger (2001) during errors of commission elicited in a degraded stimuli CPT task. This reduced activation has been interpreted as reflecting deficits in CON (Carter et al., 2001). Within their paradigm, task stimuli were degraded by removing pixels from the computer display. Using fMRI, Honey et al. (2005) have also implicated ACC dysfunction as an underlying mechanism for SCZ-related inhibitory deficits. Honey et al. (2005) employed a degraded stimuli version of the CPT to show that degradation was associated with decreased activation in the ACC (as well as decreases in the cerebellum). Individuals with SCZ also failed to show the task-specific association between the ACC and medial superior frontal gyrus (i.e., DLPFC), which was observed in healthy volunteers. This association suggests that ACC is failing to respond to the increased complexity/discriminability of task stimuli, and that the functional circuit between the ACC and DLPFC is fractured among individuals with SCZ.

Using fMRI to investigate performance on the Stroop task, Kerns, Cohen, MacDonald, Johnson, Stenger, Aizenstein, & Carter (2005) found SCZ patients to have reduced CON-related activity within the ACC. This study was important, in part, for its demonstration of reduced ACC activation on trials of conflict as well as those involving errors within the same brain region and within the same task. On post-conflict and post-error trials, SCZ patients failed to demonstrate adjustments in performance. Taken together, these findings suggest that

individuals with SCZ show impaired ACC functioning during trials of conflict and error and that such dysfunction results in a failure to make adaptive behavioural adjustments in subsequent performance (e.g., reduced RTs in congruent trials immediately following an incongruent trial). By extension, these findings also provide evidence that faulty neural circuitry, originating in the ACC (a key structure in the dorsal trend), contributes to the failure of the PFC to engage cognitive control among individuals with SCZ.

Of note, an MRI volumetric investigation implementing Nuechterlein's (1983b) degraded CPT task failed to show a significant relationship between ventral structures and inhibitory errors (Raine, 2002). This finding provides additional support for the notion that brain structures other than the IFG and OFC play a role in mediating inhibitory processes required when inhibitory cues are perceptually degraded. Collectively, behavioural and functional neuroimaging data strongly suggest that the ACC plays an important role in deciphering stimuli for use in goal directed action.

Theories of ACC functioning

The empirical findings supporting the ACC's role in deciphering and interpreting stimuli are consistent with theories that the ACC governs conflict monitoring, including operations such as response override, underdetermined responding (i.e., tasks requiring selection among equally permissible responses), and error monitoring (Braver et al., 2001; Botvinick, Nystrom, Fissell, Carter, & Cohen, 1999; Barch, Braver, Sabb, & Noll, 2000; Bunge, Hazeltine, Scanlon, Rosen, & Gabrieli, 2002; Carter, Braver, Barch, Botvinick, Noll, Cohen, 1998; Casey, Thomas, Welsh, Badgaiyan, Eccard, Jennings, Crone, deZubicaray et al., 2000; Crosson, Sadek, Bobholz, Gokcay, Mohr, & Leonard, 1999; Durston et al., 2002; Durston, Davidson, Thomas, Worden, Tottenham, Martinez Watts et al., 2003; Hazeltine,

Poldrack & Gabrieli, 2000; van Veen, Cohen, Botvinick, Stenger, & Carter, 2001; Kiehl et al., 2000; for reviews, see Botvinick, Cohen, & Carter, 2004; Ridderinkhof, Ullsperger, Crone, & Nieuwenhuis, 2004). The ACC has also been championed as the neural substrate responsible for the evaluation of action outcomes, particularly those considered aversive or those signaling reductions in reward (Gehring & Willoughby, 2002; Bush, Vogt, Holmes, Dale, Greve, Heike, & Rosen, 2002; Holroyd & Coles, 2002; Nieuwenhuis, Yeung, Holroyd, Schurger, & Cohen, 2004). The relevance of these accounts of ACC function in explaining the ACC's influence on AI, are less immediately clear. Recently, however, Botvinick (2007) has proposed a broader, integrated model of ACC functioning, which integrates these two functions (i.e., conflict-monitoring and evaluation of action outcomes). Within this revised model, conflict is registered as a cost, similar to any other perturbation that requires cognitive resources. Consequently, conflict monitoring drives a form of avoidance learning, which biases behaviour away from tasks and strategies that are prone to induce conflict, and towards those that afford relatively efficient information processing. Central to this theory is that cost is registered within the ACC, and that the ACC mediates its impact on decision making. In relation to AI, the ACC is proposed to detect conflict, allowing for the conflict-dependent allocation of inhibition (Botnivick, 2007).

Botvinick's (2007) theory has important implications for understanding SCZ, a condition routinely associated with ACC impairment. This model predicts that damage to the ACC should result in: (a) decreased ability to detect conflict, (b) decreased activation within the DLPFC on subsequent trials, and (c) a lack of behavioural adjustments commensurate with high conflict (e.g., reduced RTs on proceeding trials). For example, conflict monitoring theories of ACC were able to account for cognitive deficits observed among SCZ patients, by

suggesting that reduced ACC activation contributed, by way of faulty communication with the DLPFC, to CC deficits (Botvinick et al., 2001; van Veen & Carter, 2006).

Relationship between IFG and ACC during AI

To summarize, research indicates that the IFG plays a key role in the mediation of AI *per se*, while the ACC mediates conflict detection. Thus, the amount of AI required for a particular task is determined by the ACC, based on the amount of conflict, and the application of AI is executed by the IFG. Of relevance to the current discussion is the finding that the ACC appears particularly sensitive to manipulations which increase the ability to discriminate between task stimuli with opposing meanings (e.g., Go vs. NoGo). Such manipulations naturally increase conflict vis-à-vis these response options.

Compelling evidence for a functional and structural dissociation of AI and conflict monitoring is provided by an fMRI study by Matthews, Simmons, Arce, & Paulus (2005), in which these constructs are measured independently within the same task. Employing a SSP, Matthews et al. (2005) manipulated AI difficulty by varying SOA between the Go and the Stop signals. SOAs were individually titrated to participants' Go RTs, obtained from a previously performed SSP. In the easy AI condition, participants receive the stop signal soon after the presentation of the Go signal (i.e., Go RT minus 200, 300, 400, or 500 msec.). In the hard AI condition, participants receive the stop signal much later (i.e., Go RT or Go RT-100 msec.). When neural activation was compared across easy and hard conditions, they found increased activation in the right IFG, as well as right/left superior frontal gyrus, left lingual gyrus, right inferior tempral gyrus, and left thalamus in hard. Error-related activity was assessed by comparing neural activation between correct and incorrect stop trials. Increased neural activation was observed in the right/left dorsal ACC, as well as the right/left cuneus, right/left

postcentral gyrus, and the right fusiform gyrus during incorrect trials. These findings suggest

that AI demands and error monitoring demands are dissociable at a behavioural and anatomical

level, and that such dissociations are observable within the same paradigm.

Event-related potential (ERP) investigations have also implicated two separable ERP

components within tasks of AI: the N2 and the P3 (for review, Zordan, Sarlo, & Stablu, 2008).

The N2 component amplitude, for example, is recorded between 250 and 450 msec over

central locations during NoGo trials and is thought to constitute a marker of motor AI

(Dockree, Kelly, Robertson, Reilly, & Foxe, 2005; Falkenstein, Koshlykova, Kiroj, Noormann,

& Hohnsbeing, 1995). In contrast, the P3 component, observed on both Go and NoGo trials

and has been viewed as a marker of stimuli evaluation and/or CON resolution (Falgater &

Strik, 1999; Zordan et al, 2008; Pfefferbaum & Ford, 1988; Ford, Gray, Whitfield, Turken,

Glover, Faustman, & Mathalon, 2004).

General aims of the thesis

The purpose of the current thesis was to adapt and design cognitive paradigms in order

to orthogonally manipulate PREP and CON demands within the same AI task. The probability

of responding to a prepotent response (PREP; i.e., AI *per se*) and CON (CON) were

independently measured among individuals scoring high on the Schizotypal Personality

Questionnaire (High-SPQ) and individuals scoring in the average range on the SPQ (Ave-

SPQ). It was predicted that High-SPQs would show disproportionate impairment across

indices of increased CON with relatively intact performance across indices of increased PREP.

It was hypothesized that impairment would manifest in such conditions through (a) increased

error rates and, (b) a diminished compensatory response slowing (e.g., increased RTs) in

response to increased CON demands.

<u>Operationalization of Independent Variables</u>

Within the current thesis, CON was operationalized as the level of perceptual similarity between task stimuli representing opposing meaning. For example, within conditions of high CON (hiCON) task stimuli representing inhibitory (INH) vs. "speed up" (SU) signals (Study 1) or Go vs. NoGo signals (Study 2) had a high degree of perceptual similarity while conditions involving low CON (loCON) involved task stimuli of lower perceptual similarity.

We manipulated PREP demands by increasing ones' tendency or likelihood of depressing the response key. Notably, PREP was operationalized in different ways across the two studies. Within Study 1 this was achieved by increasing the SOA between the Go signal and the modulatory signal. It is well accepted that the later one is instructed to inhibit an action already in progress, the more difficult it is to inhibit or "cancel" that movement (Logan & Cowan, 1984). Within Study 2, PREP was manipulated by varying the ratio of Go and NoGo stimuli. It has previously been established that increasing the percentage of Go stimuli, potentiates the likelihood of incorrectly responding to NoGo stimuli (Durston et al., 2002).

Schizotypy

This thesis employed subjects with high levels of schizotypal symptoms as a representation of those with SCZ-spectrum disorders. Individuals scoring high on measures of SPD show similar clinical and cognitive characteristics to those observed among individuals with schizophrenia (see Raine, 2006, for review; Siever, Kalus & Keefe, 1993). For example, numerous studies, across diverse populations and paradigms, support the existence of a three-factor structure of SPD: cognitive-perceptual, interpersonal, and disorganized (Raine, Reynolds, Lencz, Scerbo, Triphon, & Kim, 1994; Bergman, Harvey, Mitropooulou, Aronson, Marder, Silverman, Trestman, & Siever, 1996; Battaglia, Cavallini, Macciardi, & Bellodi,

1997; Reynolds, Raine, Mellingen, Venables, & Mednick, 2000; Fossati, Raine, Carretta, Leonardi, & Maffei, 2003). This factor structure closely parallels current conceptualizations of SCZ, including the framework outlined in the DSM-IV (APA, 1994).

With regard to cognitive functioning, the deficits observed among individuals with SPD are qualitatively similar to those observed among individuals with SCZ. Specifically, they often reflect deficits in cognitive functions mediated by DLPFC such as working memory (Farmer, O'Donnell, Niznikiewicz, Voglmaier, McCarley, & Shenton, 2000; Mitropoulou, Xu, Mitropoulou, Harvey, Finch, Flory, New, et al., 2002; Mitropoulou, Harvey, Zegarelli, New, Silverman, & Siever, 2005; Park, Holzman, & Lenzenweger, 1995; Park & McTigue, 1997; Roitman, Mitropoulou, Keefe, Silverman, Serby, Harvey, Reynold, et al., 2000), attention (Bergida & Lenzenweger, 2006; Gooding, Matts, & Rollman, 2006; Lenzenweger, Cornblatt & Putnick, 1991; Chen, Zhang, & Wang, 1998; Roitman, Cornblatt, Bergman, Obuchowski, Mitropoulou, Keefe, Silverman, et al., 1997), cognitive inhibition (Beech & Claridge, 1987), dual task information processing (Harvey, Reichenberg, Romero, Graholm & Siever, 2006; Moriarty, Harvey, Mitropoulou, Grandholm, Silverman & Siever, 2003), executive functioning/cognitive control (Barch et al., 2004; Heaton, 1981; Lenzenweger & Korfine, 1992; 1994; Diforio, Walker, & Kestler, 2000; Moriarty et al., 2003; Raine et al., 2002; Trestman, Keefe, Mitropoulou, Harvey, deVegvar, Lees-Roitman, Davison, et al., 1995), and recognition memory (Cadenhead, Perry , Shafer, & Braff, 1999). Generally, the degree of cognitive impairment observed among SPDs has generally been found to be intermediate between HCs and individuals with SCZ (Trestman et al.,1995). However, others (Barch et al., 2004; Mitropoulou et al., 2005) have found more severe impairments among SPD (i.e., comparable with SCZ functioning) on tasks of working memory.

There is also some evidence that cognitive dysfunction among SPDs and those with SCZ may differ qualitatively. For example, while performance on the AX-CPT among SCZ (see Barch & Braver, 2005, for review) generally involves deficits in both context representation and maintenance, SPDs show deficits only on context representation (Barch et al., 2004). Deficits in context maintenance among SCZ, as indexed by the AX-CPT, are generally less reliable than context representation. It has been suggested that neuroleptic use rather than the pathophysiological process of SCZ *per se* contributes to impairment in context maintenance deficits in SCZ (Barch & Braver, 2005). According to this interpretation, it would be predicted that individuals with SPD, who are generally not taking neuroleptic medication, would have preserved ability to maintain context information.

Siever & Davis (2004) have proposed a model of SCZ-spectrum disorders which espouses the view that shared deficits between SCZ and SPD may reflect a common neurodevelopmentally-based cortical pathology. Although neuroanatomical investigation of SPD has been limited, the currently available findings suggest that abnormalities are intermediate between individuals with SCZ and HCs (Dickey, McCarley, & Shenton, 2002; Hazlet, Buchsbaum, Haznedar, Newmark, Goldstein, Zelmanova, Glanton, et al., 2008; Kawasaki, Suzuki, Nohara, Hagino, Takahaski, Matsui, Yamashita et al., 2004; Suzuki, Zhou, Takahashi, Hagino, Kawasaki, Niu, Matsui, Seto, & Kurachi, 2005; Takahashi, Suzuki, Zhou, Tanino, Jirofumi, Miu, Kawasaki, et al., 2006). In a recent MRI study Hazlet et al. (2008) sought to determine the extent of cortical gray and white matter volume differences between individuals with SCZ (n=79) and SPD (n=57). Hazlet et al.'s (2008) investigation was particularly important due to its inclusion of only unmedicated individuals with SCZ-spectrum disorders, a methodological rarity in previous studies. In their study, SCZ patients were found

to have significantly reduced gray matter volumes across all cortical areas examined, with marked reductions in frontal and temporal lobes. Among SPDs, reductions were found only within the frontal and temporal lobes, and to a lesser extent than observed with SCZ (i.e., approximately half).

The fact that SCZ and SPD show similar neuroanatomical, clinical, and cognitive profiles bolsters the validity of studying SPD as a representative, albeit mild, form of SCZ-spectrum disorders. Moreover, studying SPD offers several advantages over studying individuals with SCZ. Many of the potential confounds commonly observed among individuals with SCZ are not often observed among those with SPD. Due to the less severe nature of the illness, confounds such as neuroleptic medication use, hospitalization, and prolonged functional impairment, are less frequently observed among individuals with SPD. Thus, the investigation of individuals with SPD can help disentangle pathophysiological mechanisms associated with impairments in SCZ-spectrum disorders from those associated with the recurrent or chronic deficits observed in chronic SCZ (Siever & Davis, 2004).

It should be noted that definitions of schizotypy vary across studies. For example, Claridge (1994), in keeping with other British investigators, use healthy individuals whose schizotypy scores are correlated with task performance. Investigators such as Lenzenweger, Cornblatt, & Putnick (1991) and Raine (1991) favour the selection of individuals with high schizotypy scores from among large college samples. This technique was initially used by Meehl (1962) and is employed in the current thesis. In particular, Raine's (1991) suggested cut-off of 10% was used to define the High-SPQ group.

Study 1

Introduction

Theories, such as the DTT or DOH, that are embedded within evolutionary

neurobiology offer helpful frameworks within which to understand cognitive impairment

within SCZ (Christensen & Bilder, 2000; Giaccio, 2006). Within these models, SCZ-related

anomalies in cognition and behavior are posited to arise from discrepant development across

two brain pathways or trends: the archicortical dorsal trend and the paleocortical ventral trend

(Sanides, 1969; Sanides, 1972). These two related, but independent, neural pathways diverge in

architecture, connectivity, and function (Goldberg, 1985; Ungerleider & Mishkin, 1982;

Goodale & Milner, 1992; Pandya & Barnes, 1987; Pribram & McGuinness, 1975; Sanides,

1969; Sanides, 1972). With regard to function, the dorsal trend is generally thought to

subserve volitional, goal-directed behaviour that is both conscious and stable while the ventral

trend is thought to mediate the phasic interruption of ongoing goal-directed behaviour in

response to novel environment events that have emotional or motivational significance

(Christensen & Bilder, 2000; Giaccio, 2006). Various lines of evidence support the relative

sparring of ventral stream circuitry in SCZ, in the context of dorsal stream circuitry disruption

(Abruzzese et al., 1995; Abruzzese et al., 1997; Butler et al., 2001; Butler et al., 2005; Butler et

al., 2007; Cavallaro et al., 2003; King et al., 2008; O'Donnell et al., 2002; Seidman et al.,

1994; Szeszko et al., 1999).

While these theories have advanced the understanding of anomalous brain functioning

in SCZ, a persistent inconsistency exists. Specifically, individuals with SCZ are impaired on

tasks of AI such as the WCST (Gooding, Kwapil, Tallent, 1999), SSP (Badcock et al., 2002),

and Go/NoGo tasks (Kiehl et al., 2000; Rubia et al. 2001; Weisbrod, Kiefer, Marzinzik &

Spitzer, 1999). These findings run counter to the DTT and the DOH which predict relatively

intact performance on tasks mediated by the ventral trend, including tasks of AI. Notably,

evidence supporting the ventral mediation of AI, especially the IFG, has derived from several

empirical sources (for review, see Aron et al., 2003).

Here we posit a potential explanation for this inconsistency. Specifically, we suggest

that conventional AI tasks conflate AI *per se* with other cognitive processes such as CON.

Increases in CON can be realized in a variety of ways, but is often defined as any aspect of a

task which increases the difficulty of deciphering or interpreting the meaning of task stimuli

(e.g., greater perceptual similarity of task stimuli, shorter duration of stimuli presentation).

That is, the clearer the meaning of the task stimuli the easier it is for one to select the

appropriate response or action. Distinguishing between these constructs is important given

their separable neurobiological underpinnings. For example, studies implicate the IFG as the

neuroanatomical substrate of AI (for review, Aron et al., 2004), while CON is governed

principally by the ACC (ACC) (Botvinick et al., 2001; van Veen & Carter, 2006). Parsing the

unique contributions of AI and CON (and their underlying neural mechanisms) is particularly

important given that cognitive impairment among persons with SCZ is thought to be largely

mediated by structures of dorsal origin, including the ACC, while cognitive functions mediated

by neural structures of ventral origin, including the IFG, are thought to remain relatively

preserved (Christensen & Bilder, 2000; Giaccio, 2006; Butler et al. 2003; King et al., 2008).

Thus, even in the context of intact AI, individuals with SCZ may perform poorly on these

measures because of their heavy demands on CON.

In accordance with this argument are findings in which SCZ subjects are shown to be

particularly insensitive to manipulations in CON, as reflected in ACC activation. For instance,

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less than normal hemodynamic activity within the caudal ACC was observed in SCZ patients

by Carter et al. (2001) during errors of commission elicited in a continuous performance task

(CPT) (i.e., an AI task) involving degraded stimuli (i.e., hiCON). This reduced activation has

been interpreted as a reflection of SCZ patients' inability to negotiate hiCON demands (Carter

et al., 2001). Honey et al. (2005) also found decreased ACC activation in conditions of

degraded stimuli among individuals with SCZ. Persons with SCZ also failed to show the task-

specific association between the ACC and DLPFC. This association suggests that the ACC is

failing to respond to the increased CON of task stimuli, and that the functional circuit between

the ACC and DLPFC is dysfunctional among individuals with SCZ. Using fMRI to investigate

performance on the Stroop task, Kerns and colleagues (2005) also observed SCZ participants

to show abnormally reduced CON-related ACC activity and subsequent DLPFC activation.

Importantly, they also found that in post-CON trials SCZ patients failed to demonstrate

adjustments in performance (i.e., reduced RTs). Taken together, these findings suggest that, in

response to CON, individuals with SCZ show impaired functioning of the ACC, which in turn

fails to stimulate the DLPFC to engage CC, resulting in a failure to make adaptive behavioural

adjustments.

To summarize, various investigations examining the roles of the IFG and ACC suggest

that the IFG plays a key role in mediating AI *per se*, while the ACC mediates CON detection

across various tasks. Thus, the amount of AI required for a particular task is determined by the

ACC, as a function of the amount of CON inherent in a given task. Of relevance to the current

discussion is the finding that the ACC appears particularly sensitive to manipulations which

demand greater discrimination between task stimuli (i.e., greater CON) with opposing

meanings (e.g., respond vs. inhibit). Compelling findings for a functional and structural

dissociation of AI and CON is found in an fMRI study by Matthews, Simmons, Arce, & Paulus (2005), in which these constructs are measured independently within the same Go/NoGo task. Matthews et al. (2005) found increased activation in the right IFG, as well as right/left superior frontal gyrus, left lingual gyrus, right inferior temporal gyrus, and left thalamus in high AI, relative to low AI conditions. CON-related activity was assessed by comparing neural activation between correct and incorrect NoGo trials. Increased neural activation was observed in the right/left dorsal ACC, as well as the right/left cuneus, right/left postcentral gyrus, and the right fusiform gyrus during incorrect, compared to correct, trials. Overall, these findings suggest that AI demands and CON demands are dissociable at both a behavioural and anatomical level and that such dissociation is observable within the same paradigm. However, this type of within-task dissociation has yet to be examined among patients with SCZ.

The purpose of the current study is to use a modified SSP in order to examine the impact of increasing PREP and CON demands among High-SPQs. Specifically, it seeks to examine whether schizotypy is related to disproportionate AI performance decrements due to increasing CON demands, in the context of relatively preserved performance as a function of increasing PREP demands. The modifications of the SSP involve the inclusion of task stimuli which signal participants to inhibit (INH) as well as task stimuli signaling participants to speed up (SU) their response. In keeping with SSPs, our task introduces modulatory signals after the participant has initiated their response to the imperative Go stimuli. PREP is manipulated by varying the time interval between the presentation of the green circle (the Go signal) and either the INH and SU stimuli. CON is manipulated by varying the perceptual similarity between INH and SU signals. Study 1 also examines kinematic profiles associated with participants'

performance in order to ascertain fine-grained motor behavior associated with AI performance. The following are the specific hypotheses of the current study:

Within-group differences

Error rates:

1) Participants will show increased errors on inhibitory (INH) and speed-up (SU) trials in response to increases in CON and PREP.

Response times:

2) Participants will adapt to increased CON by slowing their responses (i.e., RTs on SU trials [SURTs] will increase) while adapting to increased PREP by speeding up their responses (i.e., SURTs and homekey release times [HKRTs] will decrease as PREP increases).

Kinematic analyses:

3) Participants' peak velocities will decrease in response to increased CON and increase in response to increased PREP.

Between-group differences

Error rates:

1) High-SPQs will show *disproportionately* greater error rates as CON increases, but *proportional* increases in error rates as PREP increases.

Response times:

2) High-SPQs will not reduce SURTs and HKRTs in response to the same degree as CON is increased, but will show similar decreases in SURT and HKRTs in response to increased PREP.

Kinematic Analyses:

3) High-SPQs will not reduce their peak velocities in response to increased CON, but

will increase their peak velocities proportionally in response to increased PREP.

Methods

Participants

Participants were 82 University of Waterloo (UW) undergraduate students recruited through either the Psychology department participant pool or the campus-wide participant pool during Winter and Spring 2005 semesters (refer to Appendix A). A total of 855 students were screened for this study. Eighty-five students met criteria for the High-SPQ group and 128 met criteria for the Ave-SPQ (see below for description of criteria). Of these 213 individuals, 180 were chosen randomly and contacted with an invitation to participate in the current study (refer to Appendix B, Appendix C).

The study was approved by UW's Office of Research Ethics. Participants were reimbursed for their participation through course credit, money, or a combination of both. Individuals with prominent SPD features (i.e., the High-SPQ group [n=42] were defined as those scoring in the 90th-99th%iles on the Schizotypal Personality Questionnaire (SPQ; Raine, 1991). The average scoring group, Ave-SPQ (n=40), included those scoring in the 40th – 55th%iles on the SPQ.

Participants were excluded if they self-reported: (a) neurological conditions, including loss of consciousness greater than 30 min.; (b) medical conditions with known central nervous system effects (e.g., Type I diabetes mellitus, cardiovascular disease); (c) learning disability; (d) (for Ave-SPQs only) a first-degree relative with a SCZ-spectrum disorder; or (e) (for Ave-SPQ only) a significant elevation (i.e., T score greater than 70) on any 2 clinical scales of the Personality Assessment Inventory (PAI; Morey, 2001).

In the High-SPQ group, two individuals were excluded because the computer failed to record their responses to the computer task; 1 participant was excluded because of

hypothyroidism, and 1 participant was excluded because of a history of seizures. Among the Ave-SPQ participants, 1 individual was excluded because the computer failed to record their responses, 5 were excluded because of elevations on the clinical subscales of the PAI, 1 because of heart disease, 1 because of anticholinergic medication use, and 1 because they were not part of mass-testing (see Appendix E for further details regarding study exclusion).

Materials

Clinical and neuropsychological information

In addition to completing the experimental task, various self-report and objective performance measures were completed.

The Schizotypal Personality Questionnaire (SPQ). The SPQ is a 74-item yes/no self-report comprised of 9 clinical subscales, which map onto DSM-IV symptomatology for SPD (i.e., ideas of reference, excessive social anxiety, odd beliefs/magical thinking, unusual perceptual experiences, odd/eccentric beliefs, no close friends, odd speech, constricted affect, and suspiciousness). An overall SPQ score is derived by tallying the number of positively endorsed items. The SPQ also allows for the calculation of factor scores, which can be obtained by summing the subscale raw scores for the relevant factors (e.g., Cognitive-Perceptual, Interpersonal, and Disorganized) (Raine, 1991). Participants completed the SPQ electronically as part of a larger battery of self-report measures administered online to undergraduate students volunteering as research participants.

Personality Assessment Inventory – short form (PAIsf). In addition to using the PAIsf to screen for the presence of psychopathology among Ave-SPQs, as reported above, it was also used to assess general levels of psychopathology among study participants (Morey, 1991). The

PAIsf is a 160 item abbreviated form of the Personality Assessment Inventory (Morey, 1991) requiring participants, using paper and pencil, to select from the most appropriate response (i.e., F: False, Not At All True; ST: Slightly True; MT: Mainly True; VT: Very True). Completion of this measure allows for the calculation of 4 validity scales, 11 clinical scales, 5 treatment scales, and 2 interpersonal scales.

Psychiatric Diagnostic Screening Questionnaire (PDSQ). In order to assess the presence of symptoms diagnostic of DSM-IV Axis I disorders participants completed the Psychiatric Diagnostic Screening Questionnaire (PDSQ; Zimmerman, 2000). The PDSQ provides an overall level of self-reported psychopathology, as well as an indication of whether responses meet diagnostic criteria for 13 DMS-IV Axis I disorders.

NEO Five Factor Inventory (NEO-FFI). The NEO Five-Factor Inventory (NEO-FFI) is a 60-item version of the NEO PI-R (Costa & McCrae, 1989, 1992) which calculates scores for each of the "big five" personality dimensions (i.e., extraversion, agreeableness, conscientiousness, neuroticism, and openness to experience). Given that the personality dimensions of High-SPQs has not yet thoroughly been investigated, the NEO-FFI was employed in the current study in order to help elucidate levels of the big five personality dimensions in these populations. The NEO-FFI was also used in order to uncover the presence of any unique contributions of personality dimensions on PREP and CON task demands.

Schizotypal Personality Questionnaire-B (SPQ-B). The SPQ-B is a 22 item self-report abbreviated form of the SPQ (Raine & Benishay, 1995). The SPQ-B yields a total score as well as scores for each of the three main sub-factors (i.e., cognitive perceptual, interpersonal, and disorganized). Importantly, intercorrelations between SPQ-B factors and SPQ factors range from .89 - .94 ($\underline{M}$ = .91; Raine & Benishay, 1995). In order to evaluate whether

symptoms significantly changed over time, a change score was calculated by converting participants' raw SPQ total score obtained during screening procedures weeks prior to participation and raw SPQ-B total scores, obtained during the testing session, to Z scores (see results section for further details).

Wechsler Adult Intelligence Scale – 3rd Edition (WAIS-III) subscales. The Matrix Reasoning and Information subscales of the Wechsler Adult Intelligence Scale – 3rd Edition (WAIS-III; Pearson, 1997) were administered in order to calculate an estimated Full-Scale IQ (FSIQ; Sattler & Ryan, 1999). Obtaining this measure allowed for the identification of any existing global intellectual deficits that could impact participants' performance on the experimental task.

Action Inhibition Task

The experimental task was administered to participants on a Pentium 4 DELL computer, and programmed in the $C^{\#}$ programming language. The purpose of this task was to orthogonally manipulate and measure PREP and CON task demands within the context of a modified SSP. During the task participants were seated at a table facing a computer monitor with two round black buttons, the home key and the response key (i.e., Buddy Buttons, Assistive Technologies), affixed to the table within reaching distance of the participant on the table. The distance between the edge of the table and the home key was 17.3 cm. The distance between the home key and the response key was 43 cm. The distance between the response key and the computer monitor was 21 cm. To view the apparatus layout, refer to Appendix F.

Across all conditions participants were instructed to visually focus on a fixation cross on the computer screen and, when ready, depress the black button closest to them (i.e., the home key; refer to Appendix G for complete task instructions). After the home key was

depressed, the computer screen displayed a green circle at randomly presented intervals (500, 1000, 1500, 2000, 2500, & 3000 msec) after home key depression. Randomly presented time intervals were chosen in order to prevent participants from falling into a more routinized pattern of responding, which we worried may have compromised their vigilance to detecting and deciphering task stimuli. Participants were instructed to lift and quickly move their hand toward the response key in order to make an imperative button press to the presentation of a green circle. On 60% of trials no other stimuli were presented while on 40% of the trials, a modulatory signal in the form of a box with a gap closely followed (350 or 450 msec) the presentation of the green circle.

On modulatory trials participants were instructed to either speed-up (SU) their response (i.e., when the green circle was followed by a box with a *large* gap), or inhibit (INH) their response (i.e., when the green circle was followed by a box with a *small* gap (refer to Figure 1 and Figure 2). Before beginning the experiment participants were shown the task stimuli (e.g., large vs. small gaps) in order to clarify what constituted a large vs. small gap. It was also explained that the placement of the gap may appear at any position along any side of the box.
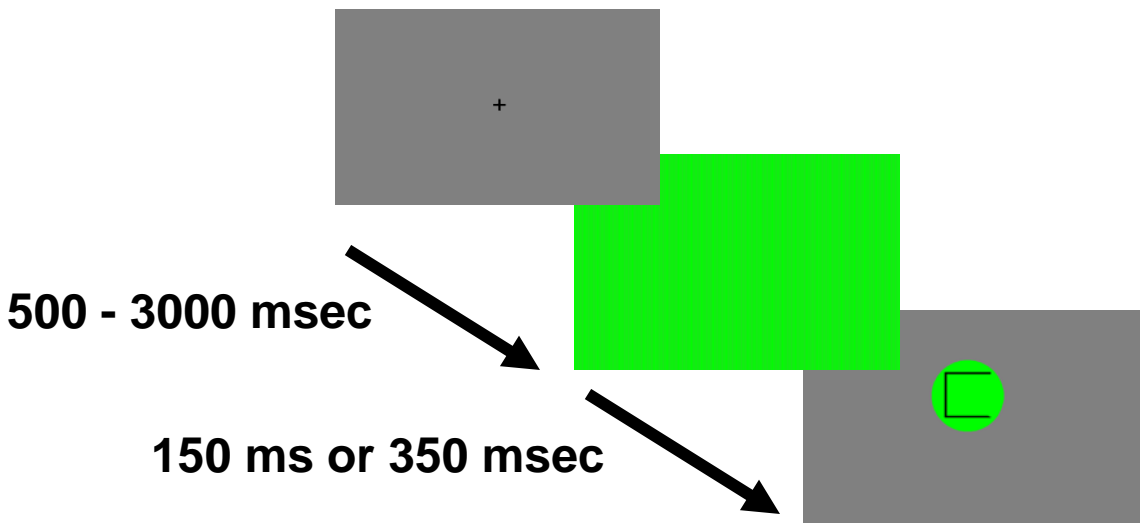
Figure 1. Sequence of visual stimuli in SU trial.
Fixation cross, followed 500 – 3000 msec by a green circle (i.e., Go signal) which signals participants to respond. Either 150 msec or 350 msec after the presentation of the green circle participants are presented with a box with a large gap (either 12% or 25% of perimeter of box) which signals participant to speed up their Go response.
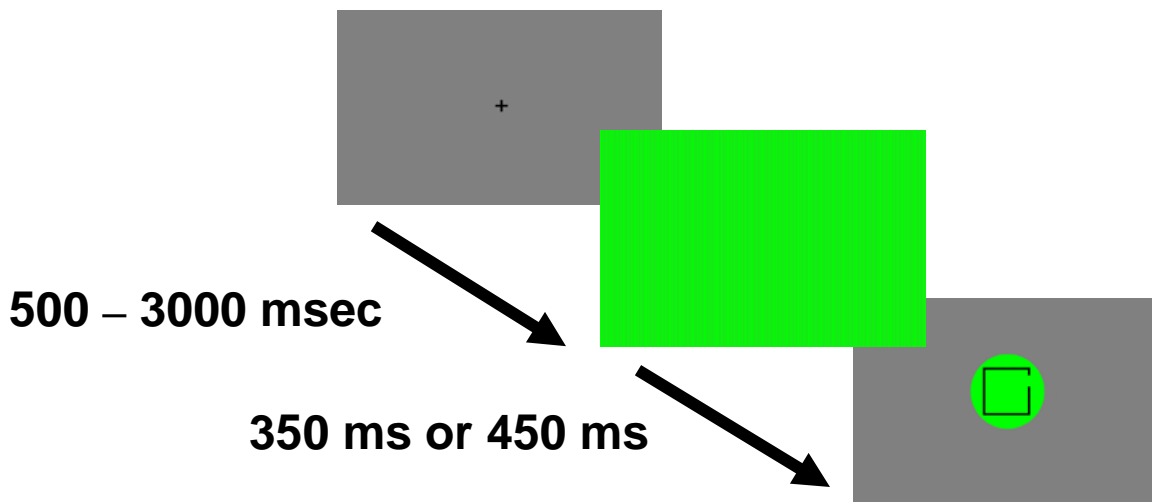
Figure 2. Sequence of visual stimuli in INH trial.
Fixation cross, followed 500 – 3000 msec by a green circle (i.e., Go signal) which signal participants to make a response. Either 350 msec. or 450 msec. after the presentation of the green circle participants are presented with a box with small gap (always 6.25% of perimeter of box) which signals participant to inhibit their Go response.

The task was presented in two blocks: high response conflict (hiCON) and low CON (loCON). CON was defined as the similarity of gap size between the SU and INH modulatory signals within a given block. The INH gap size remained constant at 6.25% across all trials. Within the loCON condition the SU gap size equaled 25% of the perimeter of the box. Within the hiCON condition the SU gap size equaled 12% of the perimeter of the box. Modulatory signal stimuli are presented in Figure 3.
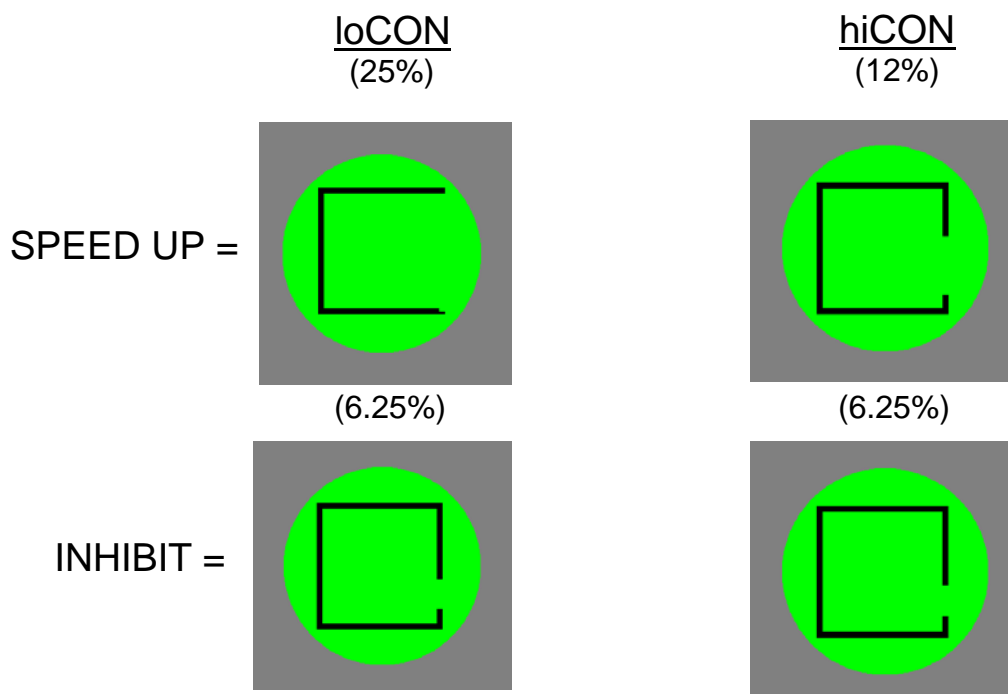
Figure 3. SU and INH gap sizes in conditions of low and hiCON.
Percentage indicates size of gap relative to total perimeter of box.

Response prepotency (PREP) (i.e., inhibition difficulty) was manipulated by varying the SOA between the presentation of the Go signal (i.e., the green circle) and the presentation of the modulatory signal (i.e., the box). Within SU trials the SOA was either 150 msec (low PREP difficulty; loPREP) or 350 msec. (hiPREP difficulty; hiPREP). Within INH trials the SOA was either 350 msec (loPREP) or 450 msec (hiPREP). Thus, PREP difficulty was

escalated by increasing the SOA between the presentation of the green circle and the modulatory signal (i.e., the box with the gap).

After each trial in which a modulatory signal was presented participants received written feedback on the computer screen. For correct SU trials the word "Good!" was presented and for unsuccessful SU trials the word, "Faster!" was presented. On correct INH trials the word, "Correct" was presented, while the word, "Incorrect" was presented on failed INH trials.

All participants were provided with 10 practice trials in order to acquaint them with task demands. Participants had the option of completing additional blocks of 10 practice trials to further familiarize themselves with the task, if so desired. In order that participants each had the same amount of exposure to modulatory signals (i.e., box with gap sizes), the words "Speed Up" (in speed up trials) or "Stop" (in INH trials) were substituted for gap sizes in the practice trials. Participants then completed an additional set of 20 practice trials, in which gap sizes were introduced as the modulatory stimuli. No feedback was provided during the practice trials (primarily because there was no baseline RT established against which to judge accuracy in SU conditions). For more detail description of task details and configurations, refer to Appendix H.

Experimental task variables

Inhibition (INH) Errors: Defined as the depression of the response key on a trial in which participants were presented with an INH signal (i.e., a box with a small gap).

Speed-Up (SU) Errors: Defined as trials in which participants were unable to decrease their response time on trials in which a SU signal was present relative to the average of the previous 10 Go trials. More specifically, if ones' RT on a SU trial (i.e., SURT) was not 3 SD

less than (i.e., quicker than) the average of the previous 10 Go trials, the response was judged an error. Trials in which no response key depression was made (i.e., an error of omission) were also considered a SU error.

Home Key Release Time (HKRT): Defined as the time between the presentation of Go signal (i.e., the green circle) and the participants' release from the home key. This measure was examined in both INH and Speed Up trials.

Response Time (RT): Defined as the time between the presentation of the Go signal (i.e., the green circle) and the participants' depression of the response key. RT was examined in Go and SU trials.

Movement Time (MT): Defined as the time between the participants' release from the home key and depression of the response key. MT is calculated by subtracting HKRT from Response Time (refer to Figure 4).
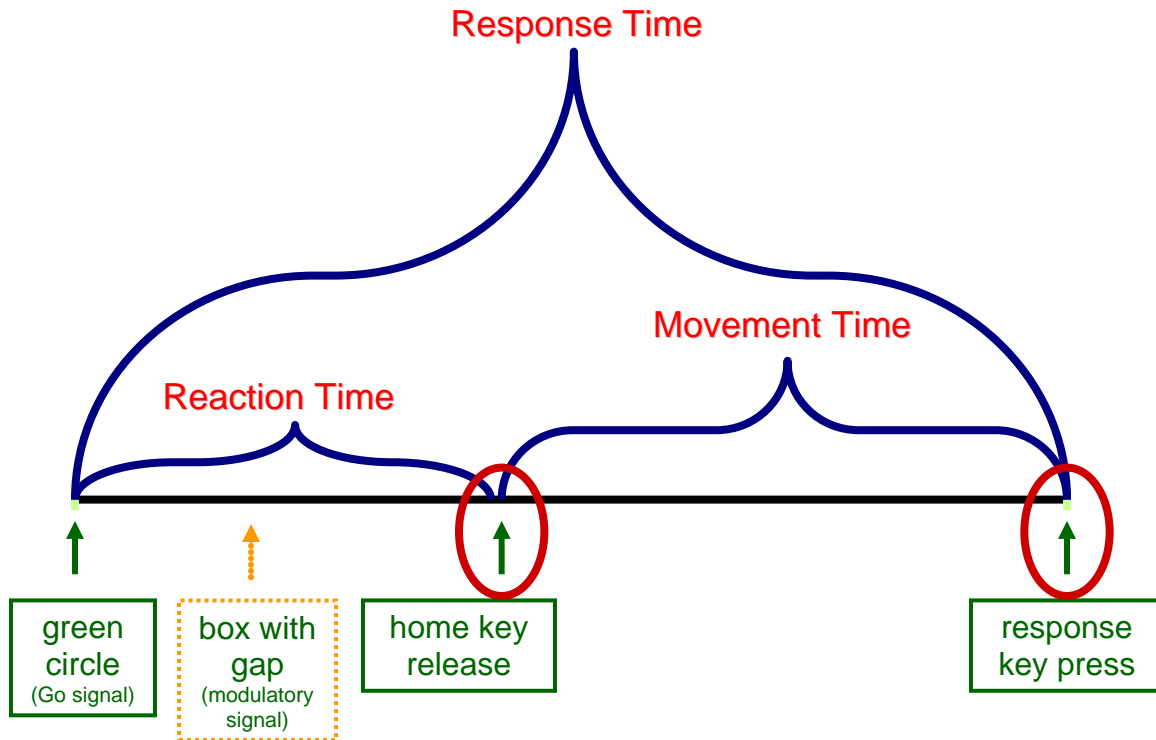
Figure 4. Schematic illustrating calculations of reaction, movement, and response time within a trial.

Kinematic measurement. Participants' hand movement during trials was recorded using a magnetic motion tracking system equipped to sample 144 measurements per second (Minibird Ascension Technology 800TM, Ascension Technology Corporation, 2000). Position data were acquired by transmitting a pulsed DC magnetic field from a transmitter unit and recording the voltage induced in 1 receiver unit that was placed on the participants' dominant hand (i.e., wrist). Position data were sampled at 144 Hz for (i.e., approximately 7 data acquisitions per second). Off-line, position data was filtered using a 10 Hz low-pass Butterworth filter, and a 2nd order dual pass. The dependent magnetic tracking variables gathered in the current study are listed below.

Movement time (MT). Defined as the time from movement onset to movement completion (i.e., depression of the response key). Therefore, the movement time represents

movement offset time minus the reaction time. Movement onset was defined as the point where wrist velocity exceeded 25 mm/sec for 5 continuous frames. Movement offset was defined by the depression of the response key.

Peak velocity (PV): Peak velocity was defined as the fastest velocity reached during movement in the x direction for the marker on the wrist.

Time to peak velocity (TPV): Defined as the time taken to reach peak velocity in the x direction.

Additional software was written in order to allow for communication between the Minibird system (via the Minibird driver) and the software application (i.e., the experimental task) at various levels of processing. First, software was written to set Minibird recording parameters. Second, software was written to record data (e.g., via the Minibird driver). Finally, software was needed to enable the synchronization of the Minibird and task parameters (e.g., FOB data acquisition began only after depression of home key). All software was written in the C[#] programming language.

Procedure

Testing took place during a two to three hour testing session in the research area of the Psychology building at UW. All participants tolerated testing well, and no threats to internal validity secondary to testing anomalies were noted. During the session, participants first completed the Action Inhibition Task (AIT). Verbatim instructions for the AIT can be found in Appendix G. Participants then completed the Psychiatric Diagnostic Screening Questionnaire, NEO-Five Factor Inventory, Personality Assessment Inventory, and Schizotypal Personality Questionnaire-B as well as a demographic questionnaire in order to ascertain relevant personal and family history. Finally participants completed the Matrix Reasoning and

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Information subscales of the WAIS-III. It is important to note that the many of the

questionnaires administered included items indicative of increased risk for suicide. For

example, the Psychiatric Diagnostic Screening Questionnaire includes the following six items

tapping suicidal ideation. Given the high rate of suicidal ideation and behaviour among this

population (e.g., estimated frequency of suicide attempts ranging from 24 – 60%; Fenton,

McGlashan, Victor, & Blyler, 1997; Borenstein, Klein, Mallon, & Slater, 1988), it is not

surprising that the PDSQ identified several of our research participants to be at an increased

risk for suicide. Consequently, it was deemed important to develop a standardized protocol

with which to assess our participants' level of risk. The risk assessment protocol is described

in Appendix I. This protocol was administered to 12 High-SPQs and 4 Ave-SPQs.

Results

Preliminary analysis

All analyses were conducted using SPSS for Windows, standard version 16.1. Prior to analysis, raw data were examined for data entry errors, missing values, and satisfaction of univariate and multivariate statistical assumptions. Data files were visually inspected for obvious mistakes and inconsistencies. Missing data were relatively rare. With regards to clinical data, the WAIS-III Information and Matrix Reasoning subtest scores were missing for 4 participants (2 Ave-SPQs and 2 High-SPQs were unable to complete the WAIS-III because of study time constraints). Among experimental data, HKRTs failed to record for 4 participants (3 High-SPQs and 1 Ave-SPQ). Among Minibird data, data capture difficulties, inherent when running the Minibird concurrently with other programs, resulted in failure of the computer to record motion data for 8 participants (5 High-SPQs and 3 Ave-SPQs), but not always across both blocks of trials (i.e., low and high RD difficulty). Each missing data point for each variable was replaced by the mean value as a function group. Of note, there were no missing data within the experimental variables of highest interest (for a more detailed description of missing data, refer to Appendix J.

The AIT data were screened for univariate normality using skewness and kurtosis values. Variables were considered non-normal if corresponding Z scores exceeded a conservative critical value ($\underline{z} > 3.08$, $\underline{p} < .001$; (Tabachnick & Fidell, 1996). Where possible, violations of kurtosis and skewness were corrected by statistical transformation (e.g., squareroot, loglinear) and are summarized in Appendix K. Generally, observed skewness and kurtosis were mild and amenable to transformations. Additionally, analyses of transformed data closely paralleled that of data from non-normalized distributions. In rare instances where

transformations were not successful in normalizing skewed and/or kurtotic distributions, non-parametric analyses were run, and found to generally closely mirror results of parametric analyses. Violations of homogeneity of variance were identified by statistically significant values (p <.05) for Levene's Test of Equality of Variances. The values for several variables were out of the acceptable range for both groups.

The presence of univariate outliers was assessed by transforming raw data to standardized scores (i.e., z scores) and examining these scores for extreme values. Scores were considered true outliers if their corresponding Z values exceeded 3.08, p<.001 (Tabachnick & Fidell, 1996) (for further details on univariate outliers, see Appendix L). Outliers for each variable were replaced by the value of the relevant variable's group mean. Multivariate outliers were assessed using Mahalanobis distance. Due to constraints in the statistical package used for the current analyses (i.e., SPSS is unable to accept 38 variables in regression analyses), the presence of multivariate outliers was explored by comparing each variable against the centroid of all remaining variables within that particular variable group (e.g., all behavioural reaction time data). The critical value for Mahalanobis distance was contingent on the number of variables included in the particular analyses and is reported below. Separate analyses were conducted for the following groups of variables: error rates, response times, HKRT, and velocity indices. In using the criterion outlined above, no multivariate outliers were identified.

Multicollinearity was assessed by examining correlation matrices of experimental variables (e.g., r >.90; Tabachnick & Fidell, 1996). The following bivariate correlations met this critical value: GoRT in hiCON condition x SU RT in hiCON, hiPREP condition (r = .934), GoRT in loCON condition x SU RT in loCON, hiPREP condition (r = .915), and SU RT in

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hiCON, hiPREP x HKRT in hiCON, loPREP condition ($\underline{r}$ = .909). The collinearity observed

between GoRTs and SURTs (in these particular conditions) is likely accounted for by a waiting

strategy used by participants when anticipating the presentation of a modulatory signal. This

strategy is explained below within the context of Study 1 results. That collinearity was also

observed between SU RT (hiCON, hiPREP) and HKRT (hiCON, loPREP) and is likely due to

the fact that HKRT is an early proxy for overall response time. Notably, no two outcome

measures within the same condition met this critical value.

<u>Demographic, neuropsychological and clinical information</u>

Demographic, neuropsychological and clinical characteristics of the sample are

presented in

Table 1. High-SPQs and Ave-SPQs did not differ on demographic variables including

age, education level, gender distribution, and handedness. They were also observed to perform

equivalently on estimated Full Scale IQ (FSIQ).

Personality Assessment Inventory – short form (PAIsf). T-scores for Negative

Impression Management (NIM) and Positive Impression Management (PIM) validity scales for

the PAIsf were generally within acceptable ranges ($\underline{T}$<92 and $\underline{T}$<68 as cut-off scores,

respectively), with the exception of two participants. One Ave-SPQ had a PIM T score of 71

while one High-SPQ had a Negative Impression Management (NIM) T score of 93. High-

SPQs demonstrated significantly higher mean T scores on several PAI scales including the

NIM, Somatization, Anxiety, Anxiety-Related Disorders, Depression, Mania, Paranoia,

Schizophrenia, Borderline, Antisocial, Alcohol, and Aggression, Suicide, and Nonsupport, but

lower on PIM, Treatment Resistance, Dominance, and Warmth.

Table 1. Demographic, clinical and neuropsychological characteristics of study 1 sample

Variables	Ave-SPQ Mean (SD) n = 32	High-SPQ Mean (SD) N = 37	Statistic	P value
Demographic:				
Age (yrs)	20.00 (2.69)	19.35 (1.38)	$t_{(1, 67)} = -1.3$	$p = .203$
Education (yrs)	14.06 (1.34)	14.00 (1.13)	$t_{(1, 67)} = -.2$	$p = .834$
%Female	71.88%	51.35%	$X^2_{(1)} = 3.0$	$p = .082$
Handedness (%right)	90.63%	100%	$x^2_{(1)} = 3.6$	$p = .057$
Neuropsychological:				
Estimated FSIQa	115.70 (11.46)	113.40 (8.90)	$t_{(1, 68)} = -.9$	$p = .352$
Clinical:				
PAI-NIM	50.03 (7.72)	62.28 (11.29)	$t_{(1, 65)} = 5.1$	$p < .001$
PAI-PIM	49.84 (6.38)	42.33 (8.58)	$t_{(1, 65)} = -4.0$	$p < .001$
PAI-SOM	46.96 (4.09)	51.22 (7.89)	$t_{(1, 54.142)} = 3.5$	$p < .001$
PAI-ANX	49.39 (6.15)	60.28 (11.61)	$t_{(1, 54.729)} = 4.9$	$p < .001$
PAI-ARD	47.55 (6.52)	59.25 (11.06)	$t_{(1, 57.947*)} = 5.4$	$p < .001$
PAI-DEP	49.19 (7.31)	61.86 (12.81)	$t_{(1, 55.844*)} = 4.9$	$p < .001$
PAI-MAN	50.35 (7.52)	55.31 (9.41)	$t_{(1, 65)} = 2.353$	$p = .022$
PAI-PAR	50.39 (6.71)	60.31 (9.46)	$t_{(1, 62.810*)} = 4.998$	$p < .001$
PAI-SCZ	48.71 (6.39)	62.83 (11.70)	$t_{(1, 55.661*)} = 6.239$	$p < .001$
PAI-BOR	50.71 (7.08)	63.25 (9.62)	$t_{(1, 65)} = 5.991$	$p < .001$
PAI-ANT	53.32 (8.58)	58.06 (10.00)	$t_{(1, 65)} = 2.061$	$p = .043$
PAI-ALC	47.26 (5.30)	52.28 (13.39)	$t_{(1, 47.063*)} = 2.069$	$p = .044$
PAI-DRG	48.10 (7.66)	51.11 (9.43)	$t_{(1, 65)} = 1.421$	$p = .160$
PAI-AGG	46.29 (6.64)	54.92 (11.24)	$t_{(1, 58.032*)} = 3.885$	$p < .001$
PAI-SUI	47.45 (4.85)	54.19 (10.56)	$t_{(1, 50.696*)} = 3.433$	$p = .001$
PAI-NS	49.10 (7.41)	61.19 (9.44)	$t_{(1, 65)} = 5.765$	$p < .001$
PAI-TR	54.03 (6.34)	45.36 (0.05)	$t_{(1, 65)} = -4.471$	$p < .001$
PAI-DOM	47.71 (0.01)	42.47 (9.44)	$t_{(1, 65)} = -2.313$	$p = .024$
PAI-WAR	50.35 (9.55)	41.14 (11.93)	$t_{(1, 65)} = -3.452$	$p = .001$

*df adjusted due to heterogeneity of variance

[a] Estimated IQ from matrix reasoning and information subtests of the WAIS-III; validity of .867 for the dyad selected (Sattler & Ryan, 1999)

PAI subscales. SOM: Somatic Complaints, ANX: Anxiety, ARD: Anxiety-Related Disorders, DEP: Depression, MAN: Mania, PAR: Paranoia, SCZ: Schizophrenia, BOR: Borderline, ANT: Antisocial Features, DRG: Drug Problems, ALC: Alcohol Problems, AGG: Aggression, SUI: Suicidal Ideation, NS: Nonsupport, TR: Treatment Rejection, DOM: Dominance, WAR: Warmth.

Schizotypal Personality Questionnaire (SPQ). High-SPQs scored significantly higher

on their total SPQ scores and across all SPQ factor scores and SPQ subscales relative to Ave-

SPQs. Notably, performance on the short form of the SPQ (SPQsf; completed during the testing session) correlated significantly with performance on the SPQ, which was completed online as part of a larger mass testing battery of questionnaires ($r = .765$, $p < .001$). Moreover, participants' Z scores on the SPQ did not significantly differ from their Z scores on the SPQ-B (t [67] = .090, $p = .929$), suggesting that the magnitude of experienced schizotypal symptoms remained relatively stable across time. Refer to Table 2 for more details.

Table 2. Schizotypal Personality Questionnaire (SPQ) scores of study 1 sample

Variables	Ave-SPQ Mean (SD) N = 32	High-SPQ Mean (SD) n = 37	Statistic	p value
SPQ Total	21.81 (4.61)	46.46 (6.96)	$t_{(1, 62.961)} = 17.541$	$p < .001$
SPQ-COG-PER	8.63 (3.28)	18.41 (5.48)	$t_{(1, 60.012)} = 9.123$	$p < .001$
SPQ-INT	9.56 (5.01)	21.76 (4.72)	$t_{(1, 64.272)} = 10.400$	$p < .001$
SPQ-DIS	5.47 (2.96)	11.65 (2.98)	$t_{(1, 67)} = 8.609$	$p < .001$
SPQ-IOR	2.81 (1.75)	6.08 (1.88)	$t_{(1, 67)} = 7.444$	$p < .001$
SPQ-ESA	3.81 (2.01)	6.35 (1.64)	$t_{(1, 67)} = 5.787$	$p < .001$
SPQ-OB/MT	1.72 (1.30)	2.65 (2.06)	$t_{(1, 61.669)} = 2.273$	$p = .027$
SPQ-UPE	2.25 (1.55)	4.32 (2.40)	$t_{(1, 62.135)} = 4.317$	$p < .001$
SPQ-OEB	1.78 (1.68)	4.46 (1.92)	$t_{(1, 67)} = 6.113$	$p < .001$
SPQ-NCF	2.09 (1.89)	5.38 (2.13)	$t_{(1, 67)} = 6.735$	$p < .001$
SPQ-OS	3.69 (2.16)	7.19 (1.71)	$t_{(1, 67)} = 7.501$	$p < .001$
SPQ-CA	1.81 (1.57)	4.68 (1.78)	$t_{(1, 67)} = 7.025$	$p < .001$
SPQ-S	1.84 (1.11)	5.35 (1.80)	$t_{(1, 60.973)} = 9.884$	$p < .001$

SPQ:
Factors: COG-PER: Cognitive Perceptual Factor, INT: Interpersonal, DIS: Disorganized
Subscales: IOR: ideas of reference, ESA: excessive Social Anxiety, OB/MG: odd behaviour/magical thinking, UPE: unusual perceptual experiences, OEB: odd/eccentric behaviour, NCF: no close friends, OS: odd speech, CA: constricted affect, S: suspiciousness.

Psychiatric Diagnostic Screening Questionnaire (PDSQ). High-SPQs were found to have significantly higher overall PDSQ scores (see Table 3). The percentage of participants meeting criteria for Generalized Anxiety Disorder ($x^2(1) = 5.176$, $p = .023$), Obsessive Compulsive Disorder ($x^2(1) = 4.740$, $p = .029$), Social Phobia ($x^2(1) = 13.6371$, $p < .001$), and Agoraphobia ($x^2(1) = 4.662$, $p = .031$) was significantly higher among High-SPQs compared to Ave-SPQs. In contrast, significant group differences were not observed when comparing the percentage of individuals meeting diagnostic criteria for Major Depressive Disorder, Panic Disorder, Posttraumatic Stress Disorder Alcohol Use, Drug Use, Psychosis, Bulimia/Binge Eating Disorder, Somatization, or Hypochondriasis.

Table 3. Psychiatric Diagnostic Screening Questionnaire (PDSQ) scores of study 1 sample

Variable	Ave-SPQ Mean (SD)/%** n = 32	High-SPQ Mean (SD)/%** n = 37	Statistic	p value
PDSQ Total	14.34 (11.60)	28.49 (15.61)	$t_{(1, 65.594)} = 4.216$	$p < .001$
PDSQ-MDD	6.25%	15.625%	$x_2(1) = .993$	$p = .319$
PDSQ-GAD	3.13%	21.62%	$x_2(1) = 5.176$	$p = .023$
PDSQ-PD	6.25%	2.70%	$x_2(1) = .519$	$p = .471$
PDSQ-PTSD	3.13%	10.81%	$x_2(1) = 1.508$	$p = .219$
PDSQ-ALC	9.38%	18.92%	$x_2(1) = 1.261$	$p = .261$
PDSQ-DRG	0.00%	8.12%	$x_2(1) = 2.713$	$p = .100$
PDSQ-PSY	3.13%	10.81%	$x_2(1) = 1.508$	$p = .219$
PDSQ-B/BED	3.13%	2.70%	$x_2(1) = .011$	$p = .917$
PDSQ-SOM	3.13%	5.41%	$x_2(1) = .215$	$p = .643$
PDSQ-OCD	18.75%	43.24%	$x_2(1) = 4.740$	$p = .029$
PDSQ-SPHO	34.38%	78.38%	$x_2(1) = 13.637I$	$p < .001$
PDSQ-HYPO	3.13%	13.51%	$x_2(1) = 2.332$	$p = .127$
PDSQ-AGOR	0.00%	13.51%	$x_2(1) = 4.662$	$p = .031$

*df adjusted due to heterogeneity of variance
** % meeting DSM-IV diagnostic criteria as per PDSQ
PDSQ subscales. MDD: Major Depressive Disorder; GAD: Generalized Anxiety Disorder' PD: Panic Disorder; PTSD: Posttraumatic Stress Disorder; ALC: Alcohol Abuse/Dependence; DTG: Drug Abuse/Dependence; PSY: Psychosis; B/BED: Bulimia/Binge-Eating Disorder; SOM: Somatization Disorder; OCD: Obsessive-Compulsive Disorder; SPHO: Social Phobia; HYPO: Hypochondriasis; AGOR: Agoraphobia

NEO Five Factor Inventory (NEO-FFI). Group means and standard deviations of Factor scores (i.e., Neuroticism, Extroversion, Openness, Agreeableness, and Conscientiousness) from the NEO-FFI are reported in Table 3. High-SPQs were found to have significantly higher levels of Neuroticism and significantly lower levels of Extroversion, Agreeableness, and Conscientiousness relative to Ave-SPQs. No significant group difference was observed on levels of Openness to Experience (see Table 4).

Table 4. NEO Five Factor Inventory scores of study 1 sample

Variables	Ave-SPQ Mean T Score (SD) n = 32	High-SPQ Mean T Score (SD) n = 37	Statistic	p value
Factor Scores:				
Neuroticism	22.09 (5.38)	31.19 (6.30)	$t_{(67)} = 6.394$	$p < .001$
Extroversion	35.41 (6.63)	29.62 (7.94)	$t_{(67)} = -3.254$	$p = .002$
Openness	34.97 (6.62)	35.19 (5.96)	$T_{(67)} = .145$	$p = .885$
Agreeableness	42.00 (5.03)	35.46 (5.37)	$t_{(67)} = -5.197$	$p < .001$
Conscientiousness	37.06 (5.47)	31.78 (6.33)	$t_{(67)} = -3.676$	$p < .001$

Action Inhibition Task data

Unless otherwise indicated, the analyses described below involved a Repeated Measures Analysis of Variance (RM-ANOVA) conducted with PREP and CON as within-subject variables and group membership (i.e., Ave-SPQ, High-SPQ) as the between-subject variable.

INH errors. As expected, the analysis revealed a significant main effect of PREP, F (1, 67) = 34.4, $p < .001$, whereby participants made significantly higher INH errors in conditions of hiPREP difficulty ($M = .38$, SD = .23) compared with loPREP difficulty ($M = .26$, SD = .18; see Figure 5). Unexpectedly, no main effect of CON was observed, F (1, 67) = 2.229, $p =$

.140, indicating that overall, participants' performance was not affected by increasing

perceptual similarity between modulatory signals (i.e., INH and SU signals) (refer to Figure 5).
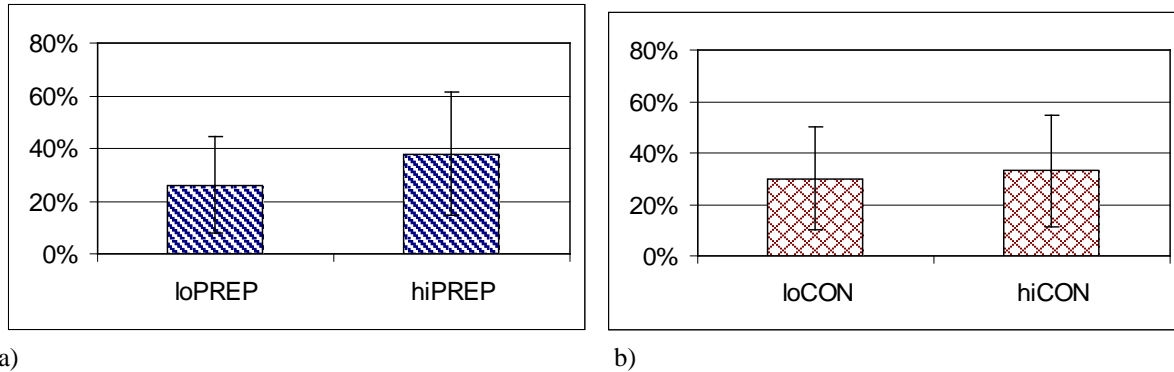
a)   b)

Figure 5. INH error rates across levels of PREP (a) and CON (b).

A significant PREP x CON interaction was observed ($\underline{F}$ (1, 67) = 17.217 $\underline{p}$ < .001),

indicating that participants made greater INH errors in conditions of hiPREP difficulty when

CON difficulty was low ($\underline{M}$ = .39, SD = .26) relative to conditions in which CON difficulty

was high ($\underline{M}$ = .36, SD = .24; $\underline{t}$ (1, 67) = 12.620, $\underline{p}$ < .001).

No significant group x PREP interaction, ($\underline{F}$ (1, 67) = .101, $\underline{p}$ = .752) or group x CON

interaction, ($\underline{F}$ [1, 67] = 2.547, $\underline{p}$ = .115) were found. Analyses did, however, show a trend

towards a significant Group x CON x PREP interaction, $\underline{F}$ (1, 67) = 3.164, $\underline{p}$ = .08. Simple

effects testing demonstrated a trend towards High-SPQs ($\underline{M}$ = .26, SD = .20) making

disproportionately greater INH errors than Ave-SPQs ($\underline{M}$ = .18, SD = .18) on trials in which

PREP difficulty and CON difficulty were low, $\underline{t}$ (1, 67) = 1.584, $\underline{p}$ = .118 (refer to Table 5);

that is, in the easiest condition when INH signals were presented at 350 msec after the

presentation of the Go signal and when perceptual similarity of INH and SU signals was low.

Notably, however, no main effect of group was observed, $\underline{F}$ (1, 67) = .292, $\underline{p}$ = .591.

Table 5. Group INH error rates across experimental conditions

Group	PREP difficulty	CON difficulty	Mean (SD)
Ave-SPQs	Low	Low	.18 (.17)
		High	.32 (.22)
	High	Low	.37 (.26)
		High	.35 (.24)
High-SPQs	Low	Low	.26 (.19)
		High	.29 (.26)
	High	Low	.41 (.26)
		High	.37 (.24)

SU errors. Although INH errors are typically the primary outcome measures of AI tasks, the logic which motivated the current study lead to the prediction that errors committed in SU conditions should also be sensitive to manipulations of PREP and CON difficulty. Specifically, if INH errors are affected by ones' ability to distinguish between INH and SU signals, it is logical to assume that ones' ability to successfully speed up ones' response time should also be impacted by ones' ability to distinguish between these same stimuli. As expected, a main effect of PREP was observed, ($\underline{F}$ (1, 67) = 80.387, $\underline{p}$ < .001), indicating that participants were less successful at speeding up their responses when PREP difficulty was high (see Figure 6). In contrast to the results obtained from INH errors, a main effect of CON was observed when examining SU errors ($\underline{F}$ (1, 67) = 15.750, $\underline{p}$ < .001), with greater SU errors on blocks in which the perceptual similarity of INH and SU signals was greater (i.e., hiCON; $\underline{M}$ = .67, SD = .25) than when modulatory signals were less similar (loCON; $\underline{M}$ = .58, SD = .25). A PREP x CON interaction was not observed, $\underline{F}$ (1, 67) = 1.765, $\underline{p}$ = .189; refer to Figure 6).

Although task manipulations of PREP and CON were partially successful in the current study, as evidenced by main effects of both PREP and CON (among SU errors), High-SPQ and

Ave-SPQ were observed to perform equivalently across these tasks. More specifically, no

main effect of group (F [1, 67] = 1.506, p = 224), no Group x PREP (F (1, 67) = 1.702, p =

.196), or Group x CON (F (1, 67) = .007, p = .934) interactions were observed. A 3-way

interaction (i.e., Group x PREP x CON) was also not observed, F (1, 67) = .812, p = .371.

Groups' mean error rates across all experimental conditions are reported in Table 6.

a)

b)
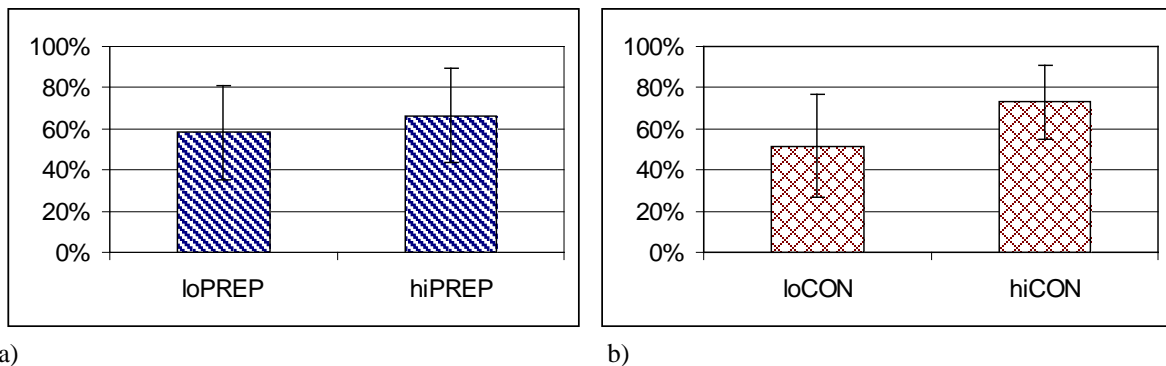
Figure 6. SU Error Rates across levels of PREP (a) and CON (b).

Table 6. Groups' SU error rates across experimental conditions

Group	PREP difficulty	CON difficulty	Mean (SD)
Ave-SPQs	Low	Low	.43 (.28)
		High	.52 (.28)
	High	Low	.68 (.19)
		High	.75 (.21)
High-SPQs	Low	Low	.50 (.28)
		High	.62 (.29)
	High	Low	.72 (.19)
		High	.77 (.21)

RTs on Go trial (GoRTs). A main effect of group was not observed, indicating that the

speed with which High-SPQs and Ave-SPQs responded to Go stimuli (i.e., the green circle), in

the absence of modulatory signals, was equivalent, F (1, 67) = 1.041, p = .311). This finding

suggests that group differences in error rate or in response times on modulatory trials are likely not accounted for by differences in general motor functioning or speed.

A significant main effect of CON, however, was observed, F (1, 67) = 11.421, p = .001, indicating that participants' GoRTs were significantly longer when embedded within trials of hiCON (M = 911.57 msec, SD = 194.33 msec) compared with loCON (M = 866.97 msec, SD = 165.21 msec). No Group x CON interaction was observed, F (1, 67) = 1.757, p = .189. Collectively these findings suggest that increasing CON between INH and SU stimuli results in increased GoRTs on non-modulatory (i.e., Go) trials. Additionally, Ave-SPQs' and High-SPQs' GoRTs appear to be affected to the same extent.

Due to inherent constraints of the task (i.e., levels of PREP were varied within the same block) it was not possible to assess GoRTs as a function of PREP difficulty. However, RTs across levels of PREP, were assessed indirectly by examining RTs on SU trials across levels of CON and PREP difficulty. Groups' mean GoRTs are reported in Table 7.

Table 7. Groups' GoRTs (in msec) across conditions of low and high CON difficulty

Group	CON difficulty	Mean (SD)
Ave-SPQs	Low	880 (164)
	High	944 (192)
High-SPQs	Low	856 (164)
	High	884 (194)

Response time on SU trials – correct trials. Please note that these analyses were conducted on only a subset of participants (i.e., only the participants who had at least 1 correct SU trial in the particular condition being analyzed). Specifically, data from 23/32 High-SPQs and 29/37 Ave-SPQs were analyzed. Group means and standard deviations across experimental conditions are reported in Table 8. A main effect of CON was observed, F (1,

50) = 5.914, $\underline{p}$ = .019, with participants showing longer RTs in SU trials (SURT) in which

CON was high. No main effect of PREP was observed, $\underline{F}$ (1, 50) = 3.083, $\underline{p}$ = .085. No PREP

x CON interaction was observed, $\underline{F}$ (1, 50) = 1.263, $\underline{p}$ = .266. No main effect of Group, $\underline{F}$ (1,

50) = 2.612, $\underline{p}$ = .112, nor a group x PREP interaction ($\underline{F}$ (1, 50) = 1.764, $\underline{p}$ = .190) or group x

PREP x CON interaction ($\underline{F}$ [1, 50] = 1.057, $\underline{p}$ = .309), were observed. There was, however, a

trend towards a significant group x CON interaction ($\underline{F}$ (1, 50) = 3.286, $\underline{p}$ = .076) with Ave-

SPQs having (marginally) longer SURTs as CON difficulty increased, relative to High-SPQs

(see Figure 7). These results suggest High-SPQs fail to reduce their speed on SU trials in the

face of increasing CON. A summary of SURT results from incorrect trials are reported in

Appendix M.

Table 8. Groups' SURTs (in msec) across experimental conditions

Group	PREP difficulty	CON difficulty	Mean (SD)
Ave-SPQs	Low	Low	788 (98)
		High	843 (135)
	High	Low	824 (174)
		High	879 (187)
High-SPQs	Low	Low	758 (98)
		High	780 (135)
	High	Low	777 (174)
		High	771 (187)

Figure 7. Response times (in msec) across levels of loCON (blue) and hiCON (red) in Ave-SPQs and High-SPQs within correct SU trials
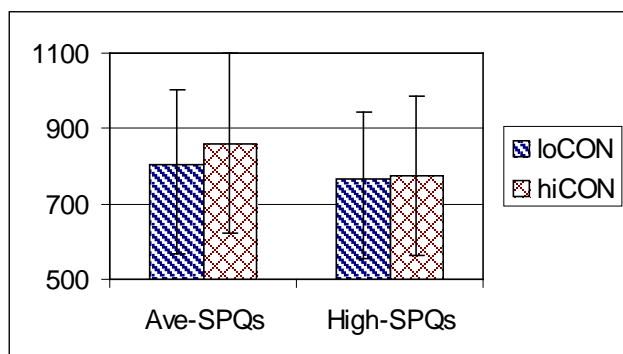
Response time in Go vs. SU trials. In order to examine the impact of the presence of modulatory signals on RTs, paired-sample t-tests were conducted to compare RTs within the two experimental blocks (i.e., SURT and GoRT in the hiCON block vs. SURT and GoRT in loCON block) with separate analyses conducted for correct and incorrect SU trials. Analyses found that participants' GoRTs (M_{CON}lo = 869.12 msec, SD_{CON}lo = 167.18 msec; $\underline{M}_{CON}$hi = 940.84 msec, SD_{CON}hi= 208.49 msec) were significantly higher than those on correct SU trials in which CON difficulty was low ($\underline{M}_{CON}$lo = 764.56 msec, SD_{CON}lo = 73.05 msec, $\underline{t}$ [1,66] = 11.716, $\underline{p}$ < .001) as well as when CON difficulty was high ($\underline{M}_{CON}$hi = 812.31 msec, SD_{CON}hi = 160.40 msec, $\underline{t}$ [1,52] = 10.475, $\underline{p}$ < .001). GoRTs were also shown to be significantly higher incorrect SURTs trials, across trials of both low ($\underline{M}_{CON}$lo = 119.99 msec, SD_{CON}lo = 16,21 msec; $\underline{t}$ [1, 62] = -10.385, $\underline{p}$ < .001) and hiCON ($\underline{M}_{CON}$hi = 1029.17 msec, SD_{CON}hi = 137.50 msec, $\underline{t}$ [1,66] = -11.752, $\underline{p}$ < .001). In summary, participants' GoRTs were significantly later across both levels of CON difficulty in both correct and incorrect SU trials. Based on the assumption that the presentation of modulatory signals would create additional cognitive processing demands, presumably leading to increased RTs, it had been assumed that RTs during the Go trials would be significantly faster than RTs in SU trials. These unexpected findings suggest that participants may have invoked a waiting strategy during task execution whereby they waited a certain period of time, likely in order to ascertain whether or not a modulatory signal would be presented, before making a response.

Home Key Response Time (HKRT). As outlined above, no group differences were observed in error rates on SU trials. However, it appears from SURTs, Ave-SPQs were differentially impacted by increases in CON difficulty. Ave-SPQ's SURTs on trials of hiCON are marginally slower than on trials of loCON. This CON effect is not observed among High-

SPQs. Instead, Ave-SPQs and High-SPQs appear similarly affected by CON difficulty level as indexed by their GoRTs (i.e., there was no group x CON interaction in GoRT). That is, within blocks of hiCON participants across both groups had significantly longer GoRTs when CON difficulty was low. This suggests that Ave-SPQs and High-SPQs may both be employing a "waiting" strategy before executing a motor response. Thus, in conditions where no modulatory signal is presented, CON difficulty impacts Ave-SPQs and High-SPQs' response times to the same degree (via the CON difficulty of the modulatory trials within that particular block). However, on trials in which a modulatory signal is present (i.e., a SU trial) Ave-SPQs, but not High-SPQs, have slower SURTs on trials of hiCON, relative to loCON.

One might expect that the slower SURTs in conditions of hiCON observed among Ave-SPQs might confer an advantage by increasing ones' chances of correctly inhibiting a prepotent response on an INH trial. However, this pattern of results was not observed (i.e., no group x CON interaction when examining INH error rates). Importantly our task differs from many AI tasks in that the response key is a relatively long distance from the home key (i.e., 43 cm). Due to this design participants are afforded a larger window of opportunity within which to "correct" their response on an INH trial. In other words, if a participant initiates movement on an INH trial by releasing their hand from the home key and accelerating towards the response key, it is possible that part way into this movement sequence the participant may recognize their response error and retract their hand before depressing the response key. Among AI tasks in which the participants' finger rests upon the response key, for example, such course corrections seem more unlikely. Given this, it is possible that participants' HKRTs may serve as an early proxy for errors of commission on INH trials. Using this logic,

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HKRTs were used to investigate whether CON had a differential impact on High-SPQs and Ave-SPQs' early movement execution.

    HKRTs within INH trials (INH HKRT) – correct trials. Within correct INH trials all participants released their hands from the home key on 100% of trials. Analysis was confined to correct trials – that is, trials in which participants' correctly refrained from depressing the home key. This allowed for analyses to be restricted to trials on which participants presumably, based on their ability to successfully inhibit depression of the response key, were intentionally inhibiting their responses. Groups' mean HKRTs within INH trials are reported in Table 9. As was seen in the SURT data, a trend towards a significant group x CON interaction was observed $\underline{F}$ (1, 65) = 3.772, p = .056 when examining INH HKRT (see Figure 8(. Specifically, relative to High-SPQs (Dif_{CON} =-1.60 msec.), Ave-SPQs (Dif_{CON} = 46.78 msec.) had a marginal increase in INH HKRTs when CON difficulty was increased. This finding suggests that the differential impact of CON on High-SPQs and Ave-SPQs is observable at an early stage of movement execution (i.e., when participants release from the home key).

Table 9. Groups' HKRT (in msec) within correct INH trials across experimental conditions

Group	PREP difficulty	CON difficulty	Mean (SD)
Ave-SPQs	Low	Low	549 (111)
		High	606 (154)
	High	Low	551 (120)
		High	587 (138)
High-SPQs	Low	Low	571 (111)
		High	563 (154)
	High	Low	570 (120)
		High	575 (138)

Figure 8. HKRTs (in msec) across levels of loCON (blue) and hi CON (red) in Ave-SPQs and High-SPQs in correct INH trials
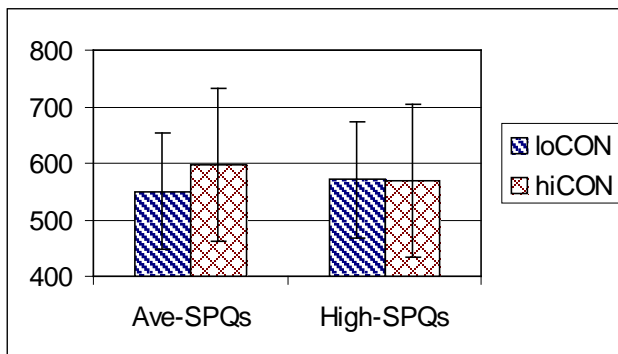
Main effects of Group ($\underline{F}$ [1, 65] = .019, $\underline{p}$ = .891), PREP ($\underline{F}$ 1, 65] = .016, $\underline{p}$ = .899), or CON ($\underline{F}$ [1, 65] = 3.291, $\underline{p}$ = .074) were not observed. PREP x Group ($\underline{F}$ (1, 65) = .563, $\underline{p}$ = .456), PREP x CON ($\underline{F}$ (1, 65) = .058, $\underline{p}$ = .811) and PREP x CON x Group ($\underline{F}$ (1, 65) = .766, $\underline{p}$ = .385) interactions were also not observed.

Collectively, GoRTs, SURTs, and SU HKRTs suggest that CON difficulty can affect task performance at various, but specific, stages of movement planning and/or execution. For example, CON difficulty appears to impact both groups' GoRTs when no modulatory signal is present (i.e., on Go trials embedded within blocks of hiCON trials); however, within SU trials, only Ave-SPQs' SURTs are affected by increased CON difficulty. Notably, these findings

leave open the possibility that separate cognitive mechanisms underlie the processing of CON

at different stages of movement planning and execution. One explanation of these data

involves the parsing of CON's impact on movement planning and execution into two levels: 1)

at the trial by trial level and 2) at the block level.

On a trial-to-trial level participants seem unaffected by CON manipulations (i.e., RT

and HKRTs not different across levels of CON difficulty). However, across blocks of trials

task performance of High-SPQs does appear to be impacted by CON manipulation.

Specifically, High-SPQs appear to invoke a waiting strategy (as do Ave-SPQs) whereby they

take longer to respond on Go trials than on trials in which a modulatory signal instructing them

to speed-up their response is presented. This suggests that High-SPQs use the CON

information to commit to a certain response style or strategy (i.e., waiting longer on blocks

when CON is high, waiting less on blocks when CON is low); however, this same information

is not used by High-SPQs within the trial to modulate responding times to SU signals of

differing degrees of CON difficulty (i.e., no difference in SU response times on trials of

loCON and hiCON).

When examining HKRT data within INH trials caution should be taken in interpreting

the current findings as participants were not explicitly told to keep their hands on the home key

during INH trials; they were only instructed to inhibit depression of the response key on INH

trials. Thus, it is difficult to interpret with any certainty the meaning of a home key release.

Although for the purposes of the current analyses a home key release has been interpreted as a

proxy for disinhibition, it is also possible that participants lift off the home key for other

reasons (e.g., boredom, to stretch).

SU HKRTs within correct trials. A main effect of group was observed, $\underline{F}$ (1, 50) = 5.553, $\underline{p}$ = .022, with High-SPQs ($\underline{M}$=439.590 msec, SD= 105.39 msec) showing faster HKRTs than Ave-SPQs ($\underline{M}$=508.944 msec, SD= 105.46 msec). A CON x group interaction was also observed in the current analyses, $\underline{F}$ (1, 50) = 7.021, $\underline{p}$ = .011, with High-SPQs ($\underline{M}$=428.77 msec, SD=74.93 msec) releasing from the home key significantly quicker than Ave-SPQs ($\underline{M}$=530.933 msec, SD=172.60 msec) only in trials of hiCON difficulty (see

Figure **9**). This finding further bolsters the notion that Ave-SPQs, but not High-SPQs, are disproportionately impacted by increasing CON difficulty.

Figure 9. Home Key Release Times (in msec) across levels of Low (blue) and High (red) CON in Ave-SPQs and High-SPQs in correct SU Ttials
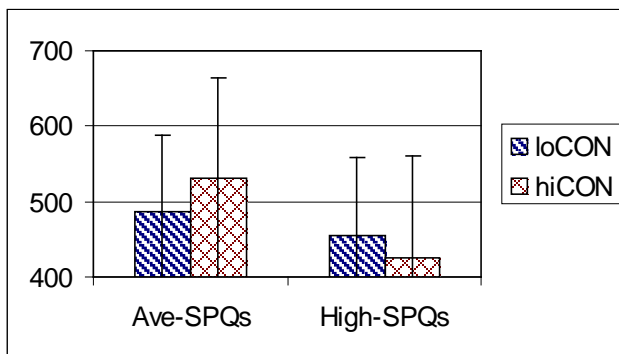
In addition, a main effect of PREP was also observed, $\underline{F}$ (1, 50) = 4.346, $\underline{p}$ = .042, with participants lifting off the home key significantly faster on trials in which PREP difficulty was high ($\underline{M}$ = 453.96 msec, SD = 124.53 msec.) compared to when it is low ($\underline{M}$ = 471.28 msec, SD = 92.77 msec). No main effect of CON was observed, $\underline{F}$ (1, 50) = .763, $\underline{p}$ = .387. Neither a PREP x group interaction ($\underline{F}$ [1, 50] = 1.357, $\underline{p}$ = .250, PREP x CON, ($\underline{F}$ [1, 50] = 1.114, $\underline{p}$ = .296), nor a PREP x CON x Group ($\underline{F}$ [1, 50] = 2.445, $\underline{p}$ = .124) interaction was observed. Groups' mean SU_HKRTs across conditions are reported in Table 10.

Table 10. Groups' SU HKRTs (in msec) across experimental conditions

Group	PREP difficulty	CON difficulty	Mean (SD)
Ave-SPQs	Low	Low	500 (82)
		High	527 (115)
	High	Low	475 (125)
		High	535 (153)
High-SPQs	Low	Low	464 (81)
		High	445 (118)
	High	Low	437 (124)
		High	412 (151)

Peak velocity within correct SU trials. In addition to examining RTs, the speed of participants' movement was assessed by examining peak velocity across experimental conditions. Although RT provides a crude indicator of speed, it does not address velocity within a trial, a measure we expected to be impacted by varying PREP and CON demands. Given that the presentation of increasingly difficult modulatory stimuli impact SURT, it seemed possible that such manipulations would also affect the speed to which participants are able to reach within a given trial.

Analyses revealed a main effect of PREP (F [1, 50] = 106.600, p < .001), with higher peak velocities observed within trials of hiPREP (i.e., when participants are presented with a "SU" signal 350 msec after the presentation of the Go signal [i.e., the green circle]; M=54.07 mm/s; SD=13.77 mm/s) compared with loPREP difficulty (i.e., when the "SU" signal was presented 150 msec after the presentation of the Go signal; M=37.71 mm/s, SD=7.86 mm/s; see Figure 10). These results suggest that the presentation of a SU signal interferes with, rather than facilitates, participants' ability to speed-up their response. For instance, if SU signals were able to facilitate an increase in velocity, one would expect greater velocities to be observed in trials in which participants are presented with the signal early, at a stage when

participants had greater time remaining in their response execution during which to increase their velocity. Our data instead support the idea that receiving a SU signal earlier in response planning/execution causes interference in participants' planning/execution of movement, leading to a decreased capacity to increase their velocity. A trend towards a main effect of CON was also found (F (1, 50) = 3.254, p = .077) with participants reaching marginally faster peak times within trials in which CON difficulty was low (M=47.19 mm/s, SD=11.39 mm/s) than when CON difficulty was high (M=44.59 mm/s, SD=10.53 mm/s; refer to Figure 10).

Table 11. Groups' Peak velocity (mm/sec) across experimental conditions

Group	PREP difficulty	CON difficulty	Mean (SD)
Ave-SPQs	Low	Low	40 (31)
		High	35 (8)
	High	Low	53 (16)
		High	49 (16)
High-SPQs	Low	Low	39 (9)
		High	36 (8)
	High	Low	57 (16)
		High	58 (16)

a)   b)
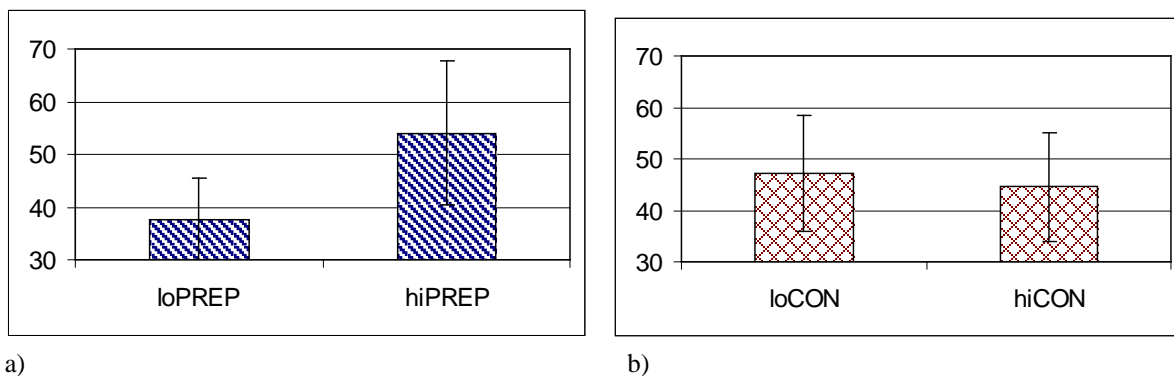
Figure 10. Peak velocity (mm/sec) across levels of PREP (a) and CON (b) difficulty

A trend towards a significant PREP x Group interaction was also observed, F (1, 50) = 3.933, p = .053, with High-SPQs (M_{PREPlo}=37.851 mm/s, SD_{PREPlo}=7.78 mm/s; M_{PREPhi}=57.347

mm/s, SD$_{PREPhi}$=13.69 mm/s) reaching higher peak velocities than Ave-SPQs (M$_{PREPlo}$=37.576 mm/s, SD$_{PREPlo}$=7.77 mm/s; M$_{PREPhi}$=50.79 mm/s, SD$_{PREPhi}$=13.72 mm/s) on high, but not low, PREP trials. This finding may suggest that High-SPQs are less able to process modulatory information at later stages of movement. No main effect of Group was observed, F (1, 50) = 1.631, p = .207. Additionally, no CON x Group (F [1, 50] = 1.530 p = .222), PREP x CON interaction (F [1, 50] = 1.622 p = .209), or PREP x CON x group interactions (F [1, 50] = 1.655, p = .204) were observed.

Time to peak velocity in correct SU trials. A main effect of PREP was observed, (F [1, 50] = 21.452, p < .001) with participants reaching their peak velocity quicker on trials of hiPREP (M=.24, SD=.10) than on trials of loPREP (M=.312, SD=.10). A main effect of CON was also observed, (F [1, 50] = 5.535, p = .023), with participants reaching their peak velocities earlier in trials of loCON (M=.261, SD= .07), relative to hiCON (M=.294, SD= .12). However, a significant PREP x CON interaction, (F [1, 50] = 5.139, p = .028) was also found showing that participants were quicker to reach peak velocity when CON was low (vs. high) only in conditions in which PREP was high (refer to Figure 11); that is, they were only quicker to reach peak velocity on trials where the perceptual similarity of INH and SU signals was low when the signals were also presented later in their movement. In contrast, no main effect of group was observed (F [1, 50] = .589, p = .446). Significant PREP x Group, (F [1, 50] = .027, p = .870), CON x Group, (F [1, 50] = .486, p = .489), and PREP x CON x Group interactions, (F [1, 50] = .007, p = .933) were also not observed.

Table 12. Groups' time to peak velocity across experimental conditions

Group	PREP difficulty	CON difficulty	Mean (SD)
Ave-SPQs	Low	Low	317 (124)
		High	322 (120)
	High	Low	212 (072)
		High	292 (168)
High-SPQs	Low	Low	313 (124)
		High	296 (118)
	High	Low	200 (075)
		High	264 (167
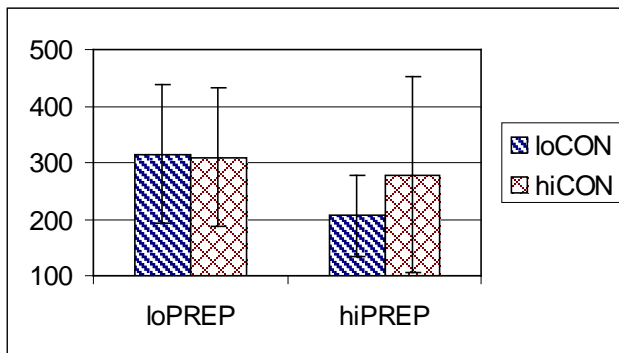
Figure 11. Time to reach peak velocity (in mm/sec) across levels of CON and PREP difficulty.

Relationship between task conditions and clinical measures

Correlational analyses were conducted (for the entire sample) between AIT experimental variables (INH errors, SU errors, GoRT, SURT, HKRT, INH and SU) and participants' responses to various clinical measures. A number of experimental (AIT) variables correlated with questionnaire data from the SPQ, the Personality Assessment Inventory, and the NEO-FFI. All significant correlations are reported in Appendix N. Interestingly, a number of significant correlations were observed when contrasting performance indices within the loPREP, loCON trial, the only condition within which Ave-SPQs and High-SPQs were observed to have marginally greater INH error rates. The number of INH errors within the loPREP, loCON condition correlated with scores on the Odd or

Eccentric Behavioural and Odd Beliefs/Magical scales as well as (in the negative direction) with the Interpersonal factor, and the Excessive Social Anxiety, No Close Friends, and Constricted Affect subscales. INH errors within this condition were also found to correlate with the Schizophrenia, Borderline, Antisocial Features, Aggression, Drug Problems, and Suicidal Ideation scales of the Personality Assessment Inventory, and with the Openness to Experience Factor (positive direction) and with the Agreeableness factor (negative direction) on the NEO-FFI.

SURTs within the loPREP, loCON condition also correlated significantly, in the negative direction with scores from the Antisocial, Aggression, Paranoia and Mania subscales of the Personality Assessment Inventory. HKRTs within INH trials of the loPREP, loCON condition correlated with the Odd or Eccentric Beliefs from the SPQ as well as the Schizophrenia and Depression subscales of the Personality Assessment Inventory. HKRT on SU trials within the loPREP, loCON condition correlated with estimated full scale IQ.

Discussion

Action Inhibition Task (AIT)

The AIT, designed to manipulate and measure PREP and CON demands independently, only partially met its objectives. As anticipated, INH error rates were greater in trials of hiPREP compared to loPREP; however, INH error rates were not observed to increase as a function of CON difficulty. In contrast, examination of SU errors revealed that manipulations of both PREP and CON impacted performance in the expected direction. It is possible that this pattern of findings can be accounted for by a "waiting" strategy employed by study participants. GoRTs were found to be significantly longer than SURTs, suggesting that participants may "wait" to view the presentation of the modulatory signal before executing or completing their responses. Notably, HKRTs across both SU and INH trials support the notion that the waiting strategy is invoked before movement execution – e.g., in conditions of hiCON, participants have significantly longer HKRT in SU trials and marginally longer HKRT in INH trials.

Invoking a waiting strategy likely serves to decrease CON demands (i.e., slowing down your response makes it easier to decipher/interpret modulatory signals, thereby decreasing CON difficulty). Importantly, however, such a strategy is likely more effective in INH trials than in SU trials; that is, it is likely easier to inhibit ones' response after waiting for the presentation of a modulatory (INH) signal than to overcome any interference effects of the modulatory (SU) signal (discussed below) in order to respond sufficiently fast. According to this rationale, increased strategy effectiveness should translate into fewer INH errors but not necessarily fewer SU errors. In keeping with this rationale increased error rates were observed as CON demands increased on SU, but not INH, trials.

Group differences

    In contrast to study hypotheses, groups were generally observed to have similar error

rates (INH and SU) across trials, with one noted exception. Specifically, within trials of

loPREP difficulty and loCON difficulty High-SPQs were observed to have greater INH errors.

These results are inconsistent with the prediction that High-SPQs would have greater error

rates as CON demands increased. They may, however, reflect an under-arousal among High-

SPQs within easy conditions, which translates into poorer performance.

    Although error rates were equivalent across groups and largely inconsistent with our

stated hypotheses, other variables did produce results suggesting a disproportionate impact of

CON on the High-SPQ group. For example, Ave-SPQs were found to have marginally longer

SURTs in conditions of hiCON but not loCON. This suggests that hiCON stimuli are used to

guide movement differentially by Ave-SPQs than by High-SPQs. For instance, it is possible

that the increased CON demands cause Ave-SPQs to slow down their response in order to

increase the decipherability of task stimuli. The RTs of High-SPQs, in contrast, appear

unaffected by increasing levels of CON difficulty. One explanation for these findings is that

High-SPQs do not detect changes to the SU stimuli (e.g., 12% vs. 25%). Alternatively, it is

possible that High-SPQs are able to perceive the differences in SU stimuli but that such

information is not used to adjust or recalibrate behaviour across levels of CON difficulty (e.g.,

when the gap is only 12% they do not slow down their response as a means of improving

performance). Regardless of how task stimuli specifically impact SURTs in the current task,

results suggest that Ave-SPQs and High-SPQs use visual task stimuli differently in order to

guide movement. Similar discrepancies in RT have previously been observed when examining

performance between individuals with SCZ and HC on the Stroop task (Kerns et al., 2005).

Kerns et al. (2005) found that individuals with SCZ failed to demonstrate adjustments in response time after experiencing CON within a task requiring inhibitory control (i.e., the Stroop). Specifically, individuals with SCZ fail to slow their RT on post-conflict and post-error trials, relative to HCs. Similarly, Carter et al. (2001) found that patients fail to significantly reduce their RTs after errors of omission on a degraded version of the AX-CPT task.

Persons with SCZ also fail to make behavioural adaptations, relative to HCs, within other tasks, such as on the pre-pulse inhibition paradigm and tasks of latent inhibition (Braff, Geyer, & Swerdlow, 2001; Kumari, Soni, & Sharma, 1999; Lubow, 2005). Within pre-pulse inhibition trials, for example, individuals with SCZ fail to reduce their startle with repeated exposure to the noxious stimuli (Braff, Geyer, & Swerdlow, 2001; Kumari, Soni, & Sharma, 1999). Latent inhibition refers to a process by which exposure to an inconsequential stimulus prevents conditioned associations with that stimulus being formed. It is believed to reflect the ability to ignore irrelevant stimuli which prevents the organism from information overload.

Functional imaging studies have shown that, among HCs, CON within AI tasks is associated with increased activation in the ACC (Kerns et al., 2004; Kok, 1986). Under similar conditions, however, persons with SCZ fail to recruit the ACC (Laurens et al., 2003; Rubia et al., 2002). Interpreting the current results within the context of these previous studies suggests possible ACC impairment within High-SPQs. Of note, the pattern of results observed in the current study is consistent with the findings anticipated by Botvinick (2007) among individuals with impaired ACC functioning. Within his model, conflict is detected by the ACC and registered as a cost, similar to any other perturbation that would require adaptation of information processing. Conflict monitoring, thought to be mediated by the ACC, is theorized

to drive a form of avoidance learning, which biases behaviour away from tasks and strategies that are prone to induce conflict, and towards those that afford relatively efficient information processing. With regards to AI, the ACC is proposed to detect conflict, allowing for a conflict-dependent allocation of inhibition (Botvinick, 2007). Decreasing ones' RT in the face of increased CON, as observed by Ave-SPQs but not High-SPQs in the current study, can be viewed as an efficient means of accommodating increased CON. Interestingly, the differential impact of increased CON demands across groups is also observed when examining HKRTs (INH and SU). That is, Ave-SPQs have higher HKRTs than High-SPQs in hiCON, but not loCON trials. Previous studies, to our knowledge, have not examined HKRTs among High-SPQs and Ave-SPQs within this context. Finding discrepancies at this initial stage of movement is significant in that it suggests that groups' RTs are, at least in part, accounted for by discrepancies in the planning of movement, rather than by differences occurring during the course of carrying out ones' response. This finding is particularly important when considering the dichotomy between the planning of a visuomotor action and its on-line control, a topic reviewed by Glover (2004). Within Glover's (2004) model, the planning system is responsible for selecting and initiating an adaptive motor program, given the environment and the goals of the actor. Within the context of the current study, the planning system would be responsible for selecting and initiating a motor program consistent with the task demands (i.e., speeding up a response when presented with a large gap and inhibiting a response when presented with a relatively smaller gap). The planning system also determines the initial kinematic parameterization of the movements, including their timing and velocity. In the current example, HKRT as well as kinematic parameters such as peak velocity and time to peak velocity (detailed below) would all be indices of the functioning of the planning system.

The control system, in contrast, provides monitoring and the occasional adjustment of motor programs in flight. These adjustments are limited to spatial characteristics of the target. The control system may intervene, for instance, if spatial errors arose for some reason (e.g., interference from cognitive influences, noise in the neuromuscular system, unexpected shift in target location). These two stages of movement are temporarily overlapping, in order to provide smooth rather than jerky movement correction. Thus, while the planning system is highly influential prior to movement initiation, and in fact, continues to by very influential early in the movement, the influence of control on the spatial parameters of the action increases.

It can also be argued that the discrepancy in HKRT between Ave-SPQs and High-SPQs within conditions of hiCON is in keeping with Botvinick's (2007) theory of ACC functioning. Specifically, the inability of the ACC to appropriately detect conflict will theoretically result in an impairment of the ACC to alert the DLPFC of such conflict. This faulty communication should presumably result in the DLPFC's failure to select motor plans appropriate for conditions of hi-CON (i.e., impact relatively early stages of response execution). Thus, the failure for High-SPQs (with presumably impaired ACC functioning) to enact behavioural adaptations appropriate for conditions of hiCON should be observed at relatively early stages of response execution.

Importantly, despite the fact that Ave-SPQs (relative to High-SPQs) appear to deal with increased CON demands by invoking a waiting strategy, groups generally have similar error rates across levels of CON difficulty. This finding is inconsistent with previous research showing that individuals with SCZ (or high-risk populations) show disproportionately higher error rates than HC as CON demands are increased on RI tasks (Nuechterlein et al., 1983a,

Nuechterlein et al., 1983b). The failure of the current study to show similar error patterns in High-SPQs may reflect the fact that participants have a 43 cm window (i.e., the distance between the home key and response key) within which they can correct/withdraw their response on INH trials. This type of course correction would not be feasible in more traditional AI tasks in which participants rest their fingers on the response button between stimuli presentations. Given this particular feature of the current task set up, INH HKRT can be considered as an early proxy for disinhibition. As noted above, High-SPQs released from the home key faster than Ave-SPQs on conditions of hiCON, but not loCON. In contrast, PREP x Group interactions were not observed when examining INH HKRTs, suggesting that groups do not differ in their response to increasing PREP demands. That is, INH HKRTs among Ave-SPQs and High-SPQs varied similarly as the SOA between the green circle and the INH signal increased. These findings are consistent with our predictions and suggest that difficulties commonly observed among persons with SCZ on tasks of RI are likely not accounted for by PREP demands.

While CON difficulty was found to differentially impact SURTs and HKRTs, group GoRTs were not found to be differentially impacted by CON manipulations. That is, both Ave-SPQs and High-SPQs were observed to show similar increases in GoRTs as CON difficulty increased even though only Ave-SPQs SURTSs increased as a function of CON difficulty. This pattern of results suggest that both groups wait for presentation of the modulatory signal in a similar fashion, but once participants are finally presented with the stimuli, Ave-SPQs react to increasing CON demands by slowing down their SURTs while High-SPQs seem impervious to such increasing demands.

Kinematic analyses

Participants were observed to have higher peak velocities within trials in which the SU signal was presented 350 msec, compared with 150 msec, after the Go signal. Our data support the idea that receiving a SU signal earlier in response planning/execution causes greater interference in participants' planning/execution of movement, leading to a decreased capacity to increase their velocity.

Manipulations in CON difficulty also impacted participants' peak velocities. Specifically, participants had marginally higher peak velocities on trials in which SU and INH stimuli was more easily distinguishable (i.e., loCON). Although no group differences were observed when assessing peak velocities overall, High-SPQs reached marginally higher peak velocities, relative to Ave-SPQs, when receiving SU signals later, rather than earlier. This finding may suggest that even when presented later, the SU signal causes interference with motor planning/execution among Ave-SPQ but not, at least to the same extent, among High-SPQs. In contrast, groups' peak velocities were not differentially impacted by increasing CON demands. To summarize, High-SPQs' responding, as indexed by their peak velocity, was less impacted by the presence of late SU signals (which are likely registered as interference by Ave-SPQ); however the degree of perceptual similarity between SU and INH signals does not differentially impact groups' peak velocities.

Participants were found to reach peak velocity more quickly on trials of hiPREP than on trials of loPREP. Participants also reached peak velocities earlier when CON demands were low. However, further analyses revealed that participants were quicker to reach peak velocity when CON was low only in conditions in which PREP was high. In other words, peak

velocities were reached earlier only when perceptual similarity between SU and INH signals was low *and* participants' prepotency to respond was, by design, highest.

Interestingly, Ave-SPQs and High-SPQs were found to need a similar amount of time to reach their peak velocities across all task conditions. These findings suggest that group differences in SURTs across levels of CON difficulty are likely due to variance in earlier movement planning and execution. In this way, the kinematic findings are consistent with the HKRT data, which also suggest that the impact of CON difficulty is observed at relatively early stages of movement execution and planning.

To the author's knowledge, no previous studies examining the kinematics of AI among individuals with SCZ-spectrum disorders have been published. Thus, the current findings help clarify both the unique contributions of PREP and CON demands at various stages of movement and planning of motor execution as well as the differential impact of such factors across Ave-SPQs and High-SPQs.

Clinical measures

High-SPQs demonstrated significantly higher mean T scores on various clinical scales of the PAI including Somatization, Anxiety, Anxiety-Related Disorders, Depression, Mania, Paranoia, Schizophrenia, Borderline, Antisocial, Alcohol, Aggression, Suicide, and Nonsupport, but lower on Positive Impression Management, Treatment Resistance, Dominance, and Warmth. High-SPQs were also found to have significantly higher overall scores on the Psychiatric Diagnostic Screening Questionnaire. The percentage of participants meeting criteria, as indexed by item endorsement on the Psychiatric Diagnostic Screening Questionnaire, was significantly higher among High-SPQs for Generalized Anxiety Disorder, Obsessive Compulsive Disorder, Social Phobia, and Agoraphobia. These findings build upon

previous literature which finds that individuals with SPD frequently meet criteria for Axis I disorders, with major affective and anxiety disorders representing a particularly common occurrence (Fenton, McGlashan, Victor et al., 1997).

High-SPQs were found to have significantly higher levels of Neuroticism and significantly lower levels of Extroversion, Agreeableness, and Conscientiousness relative to Ave-SPQs. No significant group difference was observed on levels of Openness to Experience. These results mirror previous five-factor investigations of SPD (Trull, 1992, Yeung, et al., 1993; Blais, 1997).

Relationship between task conditions and clinical measures

The majority of significant correlations between AIT variable data and clinical measures was observed when examining loPREP, loCON trials – that is, the only condition within which High-SPQs were observed to have (marginally) greater INH error rates, relative to Ave-SPQs. The number of INH errors within the loPREP, loCON condition with scores on the Odd or Eccentric Behavioural and Odd Beliefs/Magical scales as well as (in the negative direction) with the Interpersonal factor, and the Excessive Social Anxiety, No Close Friends, and Constricted Affect subscales. INH errors within this condition were also found to correlated with the Schizophrenia, Borderline, Antisocial Features, Aggression, Drug Problems, and Suicidal Ideation scales of the Personality Assessment Inventory, and with the Openness to Experience Factor (positive direction) and with the Agreeableness factor (negative direction) on the NEO-FFI. These correlations suggest that personality features (including those associated with SPD), general psychological functioning, and estimated IQ may, to some extent, contribute to performance on tasks of AI. To the author's knowledge no previous studies have examined how performance on measures such as the SPQ and PAIsf may relate to

performance on measures of AI.   Further investigations will be necessary to more fully

understand these relationships, particularly among individuals with schizophrenia-spectrum

disorders.

Limitations and future directions

The major limitation in the current study was the failure of the current paradigm to

elicit a main effect of CON within INH error rates. There appear to be two likely reasons for

this failure: first, the paradigm inadvertently allows participants to invoke a waiting strategy

which presumably decreases the impact of CON demands, in turn resulting in fewer errors.

Second, it is also possible that the hiCON condition was not sufficiently difficult (i.e., the

magnitude of the perceptual difference between the INH and SU modulatory signals was too

large). In order to address the limitations of the current paradigm, a second study was

conducted using a revised task which sought to address the limitations of the current task (i.e.,

the ease of invoking a waiting strategy and the insufficient levels of CON condition

differences).

Study 2

Introduction

In Study 1, it was hypothesized that, as CON demands increased, High-SPQs would

show   disproportionately greater error rates as well as a diminished compensatory SURT

slowing. We also predicted that as PREP demands increased, High-SPQs would demonstrate

normal modulation of their performance, exemplified by proportional increases in error rates

and decreases in SURTs. Consistent with our predictions, High-SPQs failed to reduce their

SURTs as CON demands increased (i.e., as the perceptual similarity of INH and SU signals

increased). Also consistent with our predictions was the finding that High-SPQs modified their

SURT to a similar extent compared to Ave-SPQs as PREP increased (i.e., both groups

responded quicker when SU trials represented 80%, vs. 50% of trials). Unexpectedly,

however, INH error rates among High-SPQs and Ave-SPQs were not differentially impacted

by increasing CON demands. Moreover, increasing CON difficulty did not result in increases

in INH error rates, even when examining data collapsed across groups. Participants were,

however, observed to have greater SU errors as CON increased. Despite the lack of expected

differences across all categories of error rates, results from both SURTs and HKRTs suggested

that High-SPQs and Ave-SPQs are equally affected by manipulations in PREP difficulty but

differentially impacted by increases in CON demands.

Conclusions from Study 1 regarding the impact of CON across groups are limited due

to the failure of this manipulation to result in overall increases in INH error rates. Data from

Study 1 suggested that participants were likely employing a waiting strategy before initiating

movement. Of note, slowing down ones' response time has recently been shown to be an

effective strategy to decrease inhibitory errors within SSPs (Leotti & Wager, 2010). Within

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the AIT, a waiting strategy likely serves to reduce task difficulty in two ways. First, it makes it less likely that the participant will have initiated a response at the time they receive an INH signal, thus making it easier to withhold a response. Second, waiting allows participants more time to detect and decipher the meaning of SU and INH signals, thereby indirectly decreasing the difficulty of the CON manipulation. Another potential explanation for the task's failure to elicit greater INH error rates with increased CON is simply that the CON manipulation was not sufficiently difficult.

In order to more effectively manipulate CON, Study 2 sought to address limitations of the AIT by devising and implementing a modifed version (i.e., AIT-R). Because SSPs have built-in stop-signal delays (SSD), waiting is a typical, and arguably intuitive, strategy to reduce inhibitory errors. Others have also grappled with this issue (e.g., Logan & Cowan, 1984) and in an attempt to minimize the impact of such a strategy introduced a tracking algorithm. If, for example, participants impose a delay following presentation of the go stimuli in order to monitor whether a stop signal was going to be presented, the tracking algorithm would increase the inhibitory demands of the task by increasing the SSD (Logan & Cowan, 1984).

In Study 2 we discouraged participants from using a waiting strategy through eliminating the SSD (i.e., the SOA between the presentation of the Go signal and the INH stimuli), by using a modified Go/NoGo paradigm. Within a Go/NoGo paradigm, the presentation of the INH stimuli does not follow a previously presented Go stimulus, as in the SSP. Instead, on INH trials participants view only an INH (i.e., NoGo) stimulus. Additionally, if participants slowed their RTs throughout the task, the computer would display the word, "Faster!". This is a technique used previously to discourage response slowing within the SSP (Verbruggen, Schneider, & Logan, 2008).

The AIT and AIT-R used similar task stimuli (i.e., boxes with gaps); however, within

the AIT-R CON difficulty was defined by the perceptual similarity between the Go and NoGo

stimuli whereas within the AIT CON was defined by the perceptual similarity between the INH

and SU stimuli. The perceptual similarity between these opposing signals was also greater

within the AIT-R. That is, in conditions of loCON Go was defined as a gap equal to 10% of

the box's perimeter. Within the hiCON condition Go was defined as a gap equal to 8% of the

box's perimeter. The NoGo gap was always equal to 6% of the box's perimeter (see Study 2

Methods for more detail). This discrepancy is considerably smaller than the one employed in

Study 1.

The aims of Study 2 were similar to Study 1. Specifically, we sought to independently

manipulate and measure CON and PREP difficulties within an AIT to compare performance in

Ave-SPQ and High-SPQ participants. An additional goal of Study 2, however, was to explore

the underlying genetic mechanisms of CON and PREP performance among participants with

SCZ spectrum disorders. Specifically, we tested the impact of COMT genotype on both group

membership (i.e., Ave-SPQs, High-SPQs) as well as participants' ability to manage increases

in PREP and CON demands. COMT is an enzyme that catalyses the O-methylation of

catecholamine neurotransmitters, including dopamine, a neurotransmitter system routinely

implicated in the pathophysiology of SCZ (Axelrod & Tomchick, 1958). The gene that codes

for COMT is a functional SNP that results in a val-to-met substitution. The val allele codes for

a high-activity isoform of COMT that rapidly catabolizes dopamine (DA) while the met allele

encodes a low-activity isoform of COMT (Axelrod & Tomchick, 1958). Of particular

relevance is the finding that the cognitive deficits associated with SCZ overlap with those

associated with the COMT polymorphism (Egan et al., 2001; Weinberger et al., 2001; Bilder et

al., 2002; Goldberg et al., 2003; Han et al., 2006). These associations have motivated numerous studies examining potential genetic linkage between the COMT polymorphism and SCZ, yet findings have been largely inconsistent (for review, see Glatt, Faraone, & Tsuang, 2003). For example, some studies have shown a preferential transmission of the high activity val allele to SCZ offspring (Egan et al., 2001; Li et al., 1996) while others have found no association with the disease (Karayiorgou et al., 1998; Strous et al., 1997).

With regard to cognition, the val allele of COMT has been found to be associated with poorer performance on prefrontally-mediated cognitive tasks among individuals with SCZ-spectrum disorders, such as executive functioning, processing speed, and attention (Egan et al., 2001; Weinberger et al., 2001; Bilder et al., 2002; Goldberg et al., 2003; Han et al., 2003; Minzenberg et al., 2006). Others, in contrast, have failed to show such an association (Stefanis et al., Tsai, Yu, Chen, Chen, Liou, Chen, & Hong, 2003). Bilder et al. (2004) proposed that such variability may be due, in part, to the differential effect of the COMT alleles on different types of cognitive tasks. They purport that the val allele is associated with facilitation of the switching or transitioning to alternate network states mediating the resetting of behavioural programs (i.e., facilitation of the paleocortical trend) (Bilder et al., 2004). The met allele, in contrast, is proposed to be associated with the maintenance of goal-directed behaviour (for review, see Bilder et al., 2004). Support for this model was found when examining performance on the competing paradigms task, a task which allows for the orthogonal measurement of cognitive stability and flexibility. When examining the performance of persons with SCZ on this task, Nolan et al. (2004) found that Met homozygotes performed better on aspects of the task that required cognitive stability, but greater deficit on aspects of the task that required cognitive flexibility, relative to val homozygotes.

In order to examine the association between COMT and cognitive functioning within High-SPQs and Ave-SPQs, participants' COMT genotype and performance on the AIT-R were compared. In viewing Bilder's model as consistent with the DTT, specific hypotheses (detailed below) regarding the relationship between COMT genotype and performance as a function of CON versus PREP task manipulations logically follow.

Hypothesized within group differences in AIT-R

1) Increasing CON difficulty will increase error rates (Go and NoGo) as well as RTs (GoRTs and HKRTs) in both groups.

2) Increasing PREP demands will increase NoGo and decrease Go error rates among participants in both groups and decrease (i.e., make faster) RTs (GoRTs and HKRTs) among participants in both groups.

Hypothesized between group differences in AIT-R

1) In response to increased CON demands High-SPQs will show *disproportionately greater* error rates (Go and NoGo) as well as *diminished compensatory decreases* in RTs (GoRTs and HKRTs).

2) High-SPQs will show increased error NoGo and decreased rates NoGo error rates, as well as faster RTs (GoRTs and HKRTs) *proportional* to those of Ave-SPQs.

Hypothesized associations with COMT

1) High-SPQs will show a greater representation of the val/val genotype, relative to met/met and val/met genotypes.

2) Participants with the val/val genotype will make disproportionately greater errors as CON demands increase, relative to met/met and met/val genotypes.

3) Participants with the met/met genotype will make disproportionately greater errors as PREP demands increase, relative to val/val and met/val genotypes.

Methods

Participants

Participants were 99 UW undergraduate students recruited through either the

Psychology department participant pool or the campus-wide participant pool over the Winter,

Spring, and Fall 2006 semesters and the Winter 2007 semester. A total of 3158 students were

screened for this study. Three hundred and fifteen students met criteria for the High-SPQ

group and 380 students met criteria for the Ave-SPQ group (see below for description of

inclusion and exclusion criteria). Of these 695 individuals, 110 individuals agreed to

participate in the study, 11 of whom failed to attend their scheduled testing session. Appendix

O outlines the study information made available to potential research participants on the

participant pool website. In total 98 participants completed the study protocol.

Study methods were approved by UW's Office of Research Ethics. Participants were

reimbursed for their participation through either course credit, cash payment, or a combination

of both. For study cover sheet, consent forms, debriefing/educational feedback forms, and

payment confirmation forms refer to Appendix P. The High-SPQ group (n=49) were defined

as those scoring in the 90th-99th%iles on the SPQ (SPQ; Raine, 1991). The Ave-SPQ (n=48)

included those scoring in the 40th – 55th%iles on the SPQ. The Personality Assessment

Screener (PAS; Morey, 1991) was used in order to identify Ave-SPQs with elevated levels of

psychopathology. This measure was introduced to the study protocol in the midst of

participant recruitment. The measure was administered to 2046 participants. As it was not

included in the original protocol only individuals taking part in the study in later semesters

(e.g., Spring, Fall 2006, Winter 2007) completed the PAS. The SPQ and PAS were completed

online as part of a larger battery of questionnaires administered to the entire undergraduate psychology participant pool.

Participants were excluded if they self-reported: (a) previous neurological conditions, including loss of consciousness > 30 min.; (b) medical conditions with known central nervous system effects (e.g., Type I diabetes, cardiovascular disease); (c) a diagnosis of a learning disability; (d) (for Ave-SPQs only) a first-degree relative with a SCZ-spectrum disorder; or (e) (for Ave-SPQ only) a significant elevation (i.e., T score greater than 70) on at least 1 clinical subscales of the PAI[already defined] (PAI,. Morey, 2001). To clarify, individuals scoring in the elevated range on the PAS were not invited to participate in the study. The PAI, in part, served as a secondary, more extensive screening tool, for Ave-SPQs, whose PAS scores were within normal limits and participated in the study. Among such individuals 6 participants were excluded based on elevations on PAI clinical subscales. Among Ave-SPQs, one individual was excluded because they also reported a seizure disorder, one because they had undergone neurosurgery for a blood clot, and six because they were found to have elevations on the clinical subscales of the PAI. For further details regarding study exclusion, refer to Appendix Q.

<u>Materials</u>

Clinical and neuropsychological information. In addition to completing the experimental task, various self-report and objective performance measures were completed

<u>Personality Assessment Screener (PAS).</u> The PAS (Morey, 1991) is a 22 item self-report measure which, when computed, provides a total score used to gauge the potential for clinically significant emotional and/or behavioural problems. Given the large number of individuals completing the PAS in mass testing (i.e., 3158) it would not have been feasible to

monitor and assess all individuals who endorsed suicidal ideation on the PAS. Accordingly,

the 2 PAS items probing suicidal ideation were omitted from the questionnaire when screening

potential participants. A (conservative) pro-rated cut-off was used for the purpose of screening

in the current study.

NEO Personality Inventory-Revised (NEO-PI-R). The NEO PI-R (Costa & McCrae,

1985, 1989, 1992) is a 240 item self-report measure which probes interpersonal, motivational,

emotional, and attitudinal styles. Completion of this measure allows for the calculation of each

of the "big five" personality factor scores (i.e., extraversion, agreeableness, conscientiousness,

neuroticism, and openness to experience) as well as facet scores (subscales subsumed under

each factor). It was employed in the current study in order to help characterize personality

among study participants and ultimately examine the covariation between individual

differences in personality and performance on experimental tasks.

The Personality Assessment Inventory – short form (PAIsf; Morey, 1991), the

Psychiatric Diagnostic Screening Questionnaire (PDSQ; Zimmerman, 2000), and the Matrix

Reasoning and Information subscales of the Wechsler Adult Intelligence Scale – 3rd Edition

(WAIS-III*)* were also administered. Additional information regarding these scales and the

rational for including them in the current thesis are outlined in Study 1 Methods section.

Action Inhibition Task-Revised (AIT-R)

A novel Go/NoGo task, programmed in the C# programming language, was

administered to participants on a Pentium 4 DELL computer. The purpose of the task was to

independently manipulate and measure the results from PREP and CON task demands within

the context of a modified Go/NoGo task. During the task participants were seated at a table

facing a computer monitor with two round black buttons, the home key and the response key

(i.e., Buddy Buttons, Assistive Technologies), affixed to the table within reaching distance of the participant (for picture of apparatus layout, refer to Appendix S). Across all conditions participants were instructed to visually fixate on the fixation cross on the computer screen, and when ready, depress the black button closest to them (i.e., the home key; refer to Appendix R for complete task instructions). At intervals of either 300 or 500 msec ms after the depression of the home key, the computer screen displayed a box with a gap in the middle. In response to a box with a large gap (either 8% of 10% of the box's perimeter) participants were instructed to make a Go response (i.e., hit the response key; refer to Figure 12). In response to the presentation of a box with a small gap (6% of the box's perimeter), participants were instructed to make a NoGo response (i.e., withhold from hitting the response key; see Figure 13).
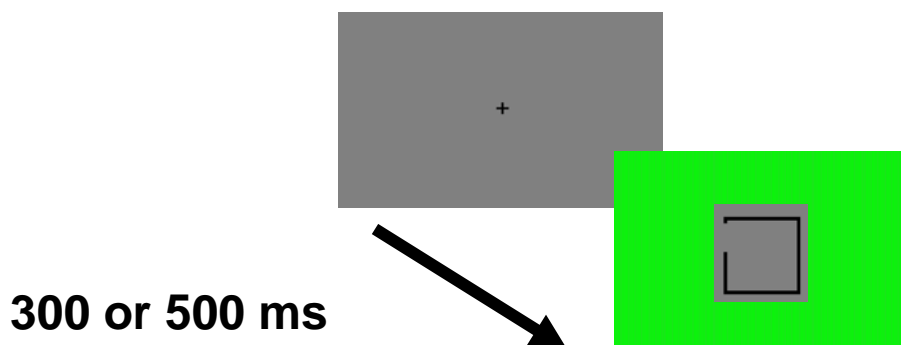
Figure 12. Sequence of visual stimuli in Go trial.

Fixation cross, followed 300 or 500 ms afterwards by a box with a large gap (either 8% or 10% of the perimeter of box); this signals participants to Go – i.e., depress the response button.
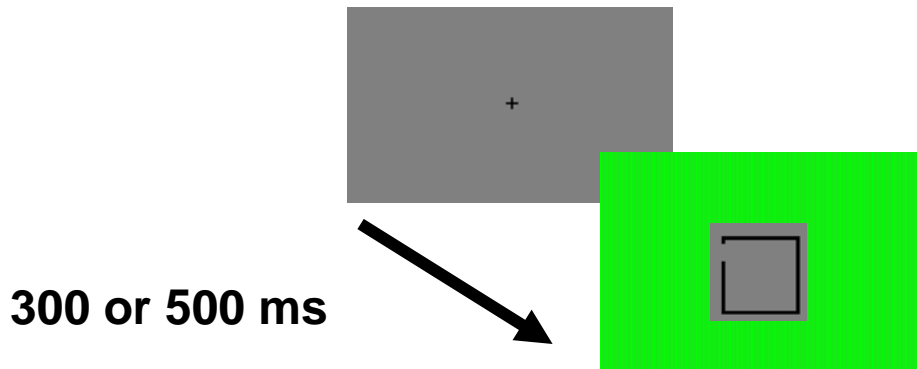
Figure 13. Sequence of visual stimuli in NoGo Trial.
Fixation cross, followed 300 or 500 ms afterwards by a box with a small gap (always 6% of the perimeter of box); this signals participants to inhibit their response.

Of note, participants were instructed to maintain depression of the home key on NoGo

trials (i.e., not to make any movements off of the home key on inhibitory trials). After each

trial, participants received feedback on their performance. Specifically, if they pressed the

response key on a Go trial or inhibited pressing the response key on a NoGo trial, the word,

"Correct" appeared on the computer screen. If participants failed to press the response key on

a Go trial or pressed the response key on a NoGo trial, the word, "Incorrect" appeared on the

computer screen.

PREP difficulty was manipulated by varying the percentage of Go trials within a block

(low difficulty = 50%, high difficulty = 80%), a technique previously shown to increase ones'

prepotency to respond to Go stimuli, thereby increasing inhibitory errors (Durston, Thomas,

Worden, Yang & Casey, 2002). CON was manipulated by varying the perceptual similarity of

the Go and NoGo gap sizes (high difficulty = gap sizes equal to 6% vs. 8% of box's perimeter;

low difficulty = 6% vs. 10%; refer to Figure 14).
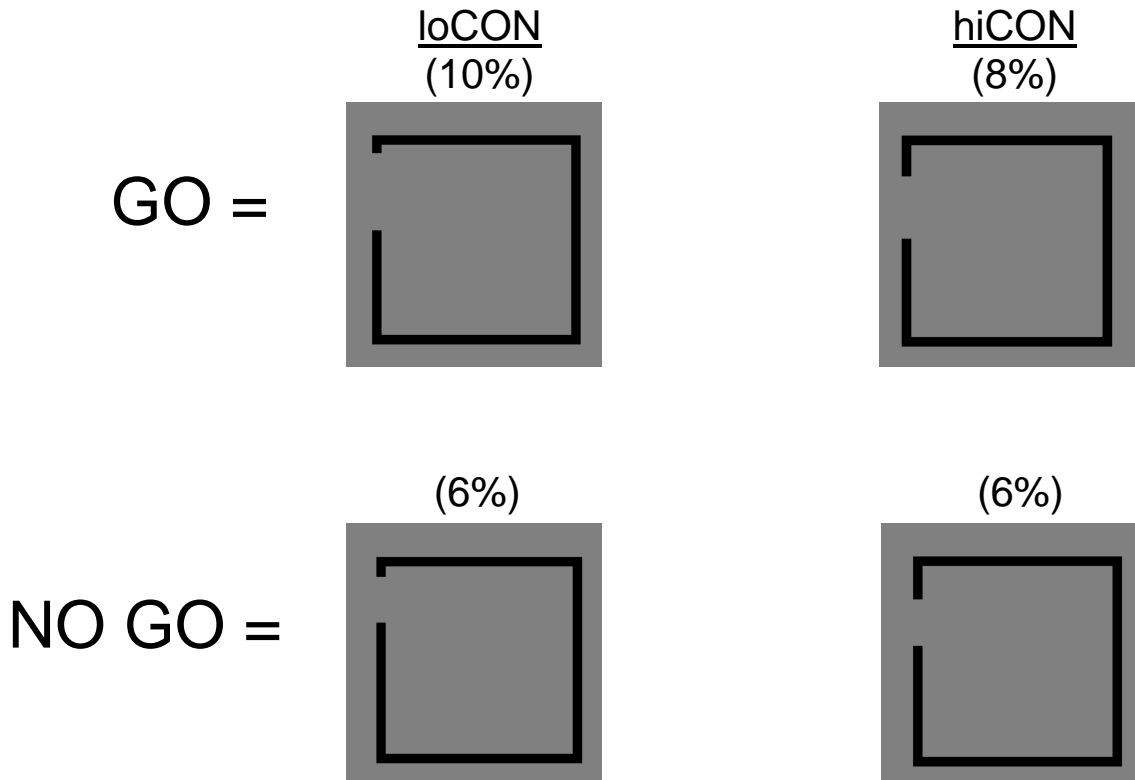
Figure 14. Go and NoGo gap sizes in conditions of loCON and hiCON difficulty.
Percentage indicates size of gap relative to perimeter of box.

All participants were provided with 10 practice trials in order to acquaint them with

task demands. Participants had the option of completing additional blocks of 10 practice trials

to further familiarize themselves with the task. In order that participants each had the same

amount of exposure to boxes with gaps, the words Go or Stop were substituted for gap sizes in

the practice Go and NoGo trials, respectively. Participants then completed an additional set of

20 practice trials, in which gap sizes were introduced as the imperative stimuli. No feedback

was provided during the practice trials. These trials also served to define baseline GoRTs, used

as a point of comparison against GoRTs in the later experimental trials. Specifically, the last

10 Go trials within the practice block were averaged to determine baseline GoRT. During

experimental Go trials, if the length of participants' RTs were 3 standard deviations above the

established baseline, the word, "Faster!" was displayed on the computer monitor at the completion of the trial. If, in contrast, participants' GoRTs on experimental trials were less than 3 standard deviations above baseline the word, "Good!" was displayed on the computer screen at the completion of the trial. The primary outcome measure was INH errors (i.e., error rate on NoGo trials); however, error rates on Go trials, GoRTs, NoGoHKRTs and GoHKRTs were also examined. The task involved four blocks of 200 trials, reflecting the 2 x 2 design (i.e., two levels of difficulty nested within the PREP and CON conditions). The four blocks were counter-balanced across participants. For an overview of task details and configurations, refer to Appendix S.

Experimental task variables

Inhibition (INH) errors. Defined as the depression of the response key on a trial in which participants were presented with a NoGo signal (i.e., a box with a small gap).

Go Errors. Defined as failure to depress the response key on a trial in which participants were presented with a Go signal (i.e., a box with a large gap).

Response Time (RT). Defined as the time between the presentation of the Go signal (i.e., a box with a large gap) and the participants' depression of the response key.

Home Key Release Time (HKRT). Defined as the time between the presentation of either the Go signal (i.e., a box with a large gap; GoHKRT) or the NoGo signal (i.e., a box with a small gap' NoGoHKRT) and the participants' release from the home key.

DNA Extraction and Analyses

DNA Extraction. DNA was collected and prepared for amplification using the MasterAmp™ Buccal Swab DNA Extraction Kit. Before sampling, participants were instructed to gently brush the inside surface of both cheeks with a toothbrush, followed by a

rinsing of the mouth with water. Next, participants were provided with a sterile buccal swab brush and instructed to roll the brush firmly up and down the inner surface of the cheek, approximately 10 times on each side in order to gather epithelial cells for analysis. The brushes were then left to air dry for 10 – 15 min. at room temperature in the testing room before samples were placed in collection tubes, then stored within a locked box at 37 degrees C.

 DNA Analysis. Samples were transported (by CMW) to the laboratory of Dr. Albert Wong (at the Centre for Addiction and Mental Health, Toronto, Canada) for DNA analysis. There tissue samples were placed into a tube containing DNA Extraction Solution. The brush was rotated a minimum of 5 times and pressed against the side of the tube and rotated while removing it from the tube to ensure that most of the liquid remained in the tube. A cap was screwed tightly onto the tube and placed on a vortex for 10 sec. and then incubated at 60 degrees C for 30 min. The mix was then vortexed for 15 sec. after which the tube was incubated at 98 degrees C for 8 min. Finally, the mix was again vortexed for 15 sec. and then chilled on ice briefly to reduce the temperature. Cellular debris was then isolated by placing the tube in the centrifuge at 4 degrees C for 5 min. The supernatant containing the DNA was then transferred to a clean tube and stored at -20 degrees C, or at -70 degrees C for longer term storage. Applied Biosystem's ™ TaqMan Polymerase Chain Reaction (PCR) assay was employed to sequence COMT Single Nucleotide Polymorphism (rs4680).

Procedure

 Testing took place during a three to four hour testing session in the research area of the Psychology Building at UW. All participants tolerated testing well, and no threats to internal validity secondary to testing anomalies were noted. During the session, participants first

provided a DNA sample (i.e., a cheek swab), then completed the AIT-R. Verbatim instructions

for the AIT-R can be found in Appendix R. Participants then completed a series of self report

measures (i.e., PDSQ, NEO-PI-R, PAI, and PSQ-B) as well as a demographic questionnaire.

Finally participants completed the Matrix Reasoning and Information subscales of the WAIS-

III. If participants' questionnaire responses indicated risk of suicide, a risk assessment was

undertaken (see Appendix I for details).

Results

Preliminary analysis

All preliminary analyses in Study 2 were conducted in the same manner as in Study 1. Please refer to Study 1 Results section for a detailed explanation of analyses undertaken. Missing data were relatively rare. With regards to clinical data, the WAIS-III information and matrix reasoning subtest scores were missing for 4 High-SPQ participants who were unable to complete these measures because of study time constraints. The PAIsf was also missing for 1 Ave-SPQ because of time constraints. The NEO-PI-R was missing for 4 High-SPQs and 1 Ave-SPQ. Each missing data point for each variable was replaced by mean group values. For a more detailed description of missing experimental data, refer to Appendix T. Univariate outliers are reported in Appendix U. Outliers for each variable were replaced by the value of the relevant variable's group mean. Where possible, violations of kurtosis and skewness were corrected by statistical transformation (e.g., squareroot, loglinear) and are summarized in Appendix V. Transformed data closely paralleled that of data from normalized distributions. In instances where transformations were not successful in normalizing skewed and/or kurtotic distributions, non-parametric analyses were conducted, and were generally found to mirror results of parametric analyses. No multivariate outliers were identified. Multicollinearity was assessed by examining correlation matrices of experimental variables. No study variables met criteria for multicolinearity.

Demographic, neuropsychological and clinical information

Demographic, neuropsychological and clinical characteristics of the sample are

presented in Table 13. High-SPQs and Ave-SPQs did not differ on various demographic

indices including age, education level, gender distribution, and handedness. They were also

observed to perform equivalently on an estimate of FSIQ.

Table 13. Demographic, clinical and neuropsychological characteristics of study 2 sample

Variables	Ave-SPQ Mean (SD) n = 40	High-SPQ Mean (SD) n = 48	Statistic	p value
Demographic:				
Age	19.58 (1.72)	19.52 (2.26)	$t_{(86)} = -.124$	$p = .901$
Education	14.18 (1.58)	13.85 (1.11)	$t_{(68.047)*} = -1.079$	$p = .284$
Gender (% Female)	55%	63%	$x^2_{(1)} = .382$	$p = .537$
Handedness (% Right)	95%	92%	$x^2_{(1)} = .508$	$p = .476$
Neuropsychological:				
Estimated FSIQ	115.05 (11.88)	110.86 (11.79)	$t_{(86)*} = -1.652$	$p = .102$

*df adjusted due to heterogeneity of variance

Personality Assessment Inventory (PAI)

T-scores for negative impression management (NIM) and positive impression

management (PIM) scales were generally within acceptable ranges (T<92 and T<68 as cut-off

scores, respectively), with the exception of two participants. One Ave-SPQ had a PIM T score

of 71 and one High-SPQ had a PIM of 71. Two High-SPQs had a NIM T scores greater than

92 (i.e., 116, 93). These participants' PAIsf scores were excluded from analysis. Group T

score means and standard deviations are reported in Table 14. High-SPQs demonstrated

significantly higher mean T scores on several indices of the PAI including NIM, Somatization,

Anxiety, Anxiety-Related Disorders, Depression, Mania, Paranoia, Schizophrenia, Borderline,

Antisocial, Alcohol, Suicide, and Nonsupport, but lower on indices of PIM, Treatment

Resistance, Dominance, and Warmth.

Table 14. PAI clinical scale group means and standard deviations of study 2 sample.

Variables	Ave-SPQ Mean (SD) n = 39	High-SPQ Mean (SD) n = 45	Statistic	p value
PAI Clinical Subscale:				
PAI-Nim	47.68 (4.17)	60.24 (13.46)	$t_{(53.99)*} = 5.522$	$p < .001$
PAI-Pim	51.00 (8.26)	41.58 (9.43)	$t_{(81)} = -4.774$	$p < .001$
PAI-Som	45.18 (2.74)	50.09 (6.15)	$t_{(63.463)*} = 4.804$	$p < .001$
PAI-Anx	46.18 (4.94)	61.69 (14.12)	$t_{(56.595)*} = 6.874$	$p < .001$
PAI-ARD	45.89 (7.88)	60.09 (12.75)	$t_{(75.096)*} = 6.170$	$p < .001$
PAI-Dep	46.05 (6.23)	64.29 (15.98)	$t_{(59.362)*} = 7.031$	$p < .001$
PAI-Man	49.39 (7.36)	55.53 (12.48)	$t_{(73.492)*} = 2.766$	$p = .007$
PAI-Par	47.63 (6.99)	59.56 (10.20)	$t_{(81))} = 6.070$	$p < .001$
PAI-Scz	47.16 (6.13)	66.18 (14.58)	$t_{(61.582)*} = 7.939$	$p < .001$
PAI-Bord	49.18 (8.07)	64.31 (10.52)	$t_{(81)} = 7.210$	$p < .001$
PAI-Anti	49.47 (7.00)	56.60 (12.87)	$t_{(70.487)*} = 3.186$	$p = .002$
PAI-Alc	46.47 (3.82)	50.82 (12.36)	$t_{(53.927)*} = 2.233$	$p = .030$
PAI-Dru	48.26 (7.10)	49.67 (6.96)	$t_{(81)} = .901$	$p = .370$
PAI-Agg	46.16 (6.77)	49.42 (11.03)	$t_{(74.868)*} = 1.643$	$p = .104$
PAI-Sui	48.26 (6.31)	56.38 (14.53)	$t_{(62.607)*} = 3.378$	$p = .001$
PAI-NS	48.89 (8.42)	60.16 (11.54)	$t_{(81)} = 4.975$	$p < .001$
PAI-RR	53.71 (9.27)	42.13 (9.83)	$t_{(81)} = -5.474$	$p < .001$
PAI-Dom	49.37 (8.76)	42.24 (9.87)	$t_{(81)} = -3.430$	$p = .001$
PAI-War	51.61 (9.83)	41.89 (10.49)	$t_{(81)*} = -4.301$	$p < .001$

*df adjusted due to heterogeneity of variance.
PAI: Personality Assessment Inventory (PAI); Nim: Negative Impression Management; PIM: Positive Impression Management; Som: Somatization; Anx: Anxiety; ARD: Anxiety-Related Disorder; Dep: Depression; Man: Mania, Par: Paranoia; Scz: Schizophrenia; Bord: Borderline; Anti: Antisocial; Alc: Alcohol; Dru: Drug Use; Agg: Aggression; Sui: Suicide; NS: Non-Support; RR: Reaction Resistance; Dom: Dominant; War: Warmth.

High-SPQs scored significantly higher on their total SPQ scores as well as across all SPQ factor and subscale scores, relative to Ave-SPQs (Table 15). Their performance on the short form of the SPQ (SPQ-B; completed during the face-to-face testing session) correlated significantly with performance on the SPQ, which was completed online as part of a larger mass testing battery of questionnaires ($r = .666$, $p < .001$). Participants' Z scores on the SPQ did not significantly differ from their Z scores on the SPQ-B (t (86) = -.213, $p = .832$) suggesting that the magnitude of experienced schizotypal symptoms did not differ across time.

Table 15. SPQ and SPQ-B group means and standard deviations of study 2 sample.

Variable	Ave-SPQ Mean (SD) n = 40	High-SPQ Mean (SD) n = 48	Statistic	p value
SPQ Total	19.85 (2.39)	47.88 (8.82)	$t_{(55.150)*} = 21.110$	$p < .001$
SPQ B[i]	5.13 (2.55)	12.81 (4.87)	$t_{(73.660)*} = 9.461$	$p < .001$
SPQ Factors				
SPQ-Cog-Per	8.35 (4.12)	19.23 (5.52)	$t_{(83.665)*} = 10.504$	$p < .001$
SPQ-Int	8.68 (3.80)	22.21 (5.43)	$t_{(82.080)*} = 13.614$	$p < .001$
SPQ-Dis	4.68 (2.53)	11.79 (3.06)	$t_{(85)} = 11.701$	$p < .001$
SPQ subscales				
SPQ-IOR	6.42 (1.91)	3.10 (1.95)	$t_{(86)} = 8.041$	$p < .001$
SPQ-ESA	3.25 (2.44)	6.69 (1.36)	$t_{(58.477)*} = 7.956$	$p < .001$
SPQ-OB/MT	1.40 (1.34)	2.75 (1.88)	$t_{(83.969)*} = 3.919$	$p < .001$
SPQ-UPE	2.00 (1.55)	4.60 (2.18)	$t_{(84.078)*} = 6.524$	$p < .001$
SPQ-OEB	1.40 (1.82)	4.88 (1.67)	$t_{(86)} = 9.320$	$p < .001$
SPQ-NCF	1.98 (2.09)	5.52 (2.19)	$t_{(86)} = 7.709$	$p < .001$
SPQ-OS	3.28 (1.65)	6.92 (2.01)	$t_{(86)} = 9.174$	$p < .001$
SPQ-CA	1.60 (1.46)	4.65 (1.91)	$t_{(86)} = 8.269$	$p < .001$
SPQ-S	1.85 (1.29)	5.46 (1.90)	$t_{(82.857)*} = 10.857$	$p < .001$

i SPQ-B: the Shortened version of the SPQ administered during face-to-face testing session
*df adjusted due to heterogeneity of variance
SPQ: Schizotypal Personality Questionnaire (SPQ); Cog-Per: Cognitive Perceptual; Int: Interpersonal; Dis: Disorganized; IOR: Ideas of Reference; ESA: Excessive Social Anxiety; OB/MT: Odd Beliefs/Magical Thinking; UPE: Unusual Perceptual Experiences; OEB: Odd Eccentric Beliefs; NCF: No Close Friends; OS: Odd Speech; Constricted Affect; CA: S: Suspiciousness.

NEO-Personality Inventory-Revised (NEO-PI-R)

High-SPQs and Ave-SPQs were observed to vary across various factor and facet scores. Group Means and standard deviations for the NEO-PI-R are reported in Table 16. With regards to Factor scores, High-SPQs obtained higher scores on Neuroticism. All facet scores within Neuroticism (i.e., anxiety, angry hostility, depression, self-consciousness, impulsivity, and vulnerability) were also significantly elevated in High-SPQs. In contrast, High-SPQs had significantly lower scores on the Extroversion, Agreeableness, and Conscientiousness Factors. Within Extraversion, High-SPQs obtained significantly lower scores on the facets Warmth, Gregariousness, Assertiveness, Positive Emotions and (marginally) Activity, but not Excitement-Seeking. Within the domain of Agreeableness, High-SPQs had significantly lower scores on the facets Trust, Altruism, and (marginally) Straightforwardness, but not Compliance, Honesty, and Tendermindedness. On Conscientiousness facets, High-SPQs scored significantly lower on measures of Competence, Dutifulness, Achievement-Striving, Deliberation, Self-Discipline, but not Order. A group difference was not observed on the Openness to Experience Factor. Generally, the facets within this domain (i.e., Fantasy, Aesthetics, Feelings, Actions, Ideas) also did not differ as a function of group membership. High-SPQs were, however, observed to have marginally lower scores on the Values facet.

Table 16. NEO-PI-R Factor and Facet Scores of Study 2 Sample

Variables	Ave-SPQ Mean T Score (SD) n = 40	High-SPQ Mean T Score (SD) n = 48	Statistic	P value
NEO Score:				
Neuroticism (N) Factor	49.51 (10.24)	63.21 (7.94)	$t_{(86)} = 7.067$	$p < .001$
N-Anxiety	46.74 (8.37)	56.76 (8.71)	$t_{(86)} = 5.467$	$p < .001$
N-Angry Hostility	47.80 (10.30)	56.69 (10.20)	$t_{(86)} = 4.055$	$p < .001$
N-Depression	46.83 (10.21)	62.88 (9.75)	$t_{(86)} = 7.528$	$p < .001$
N-Self-Consciousness	49.41 (11.62)	61.29 (10.48)	$t_{(86)} = 5.039$	$p < .001$
N-Impulsiveness	51.48 (6.60)	54.90 (7.13)	$t_{(86)} = 2.318$	$p = .023$
N-Vulnerability	57.66 (10.35)	67.64 (8.17)	$t_{(86)} = 5.039$	$p < .001$
Extroversion (E) Factor	54.37 (11.38)	46.15 (11.33)	$t_{(86)} = -3.384$	$p = .001$
E-Warmth	50.69 (11.74)	42.70 (9.80)	$t_{(86)} = -3.477$	$p = .001$
E-Gregariousness	56.08 (12.87)	46.20 (12.66)	$t_{(86)} = -3.620$	$p < .001$
E-Assertiveness	51.75 (8.00)	48.34 (7.40)	$t_{(86)} = -2.075$	$p = .041$
E-Activity	49.58 (9.25)	45.32 (10.80)	$t_{(86)} = -1.965$	$p = .053$
E-Excitement Seeking	55.90 (8.63)	55.73 (9.61)	$t_{(86)} = -.086$	$p = .931$
E-Positive Emotions	52.91 (11.01)	44.32 (12.28)	$t_{(86)} = -3.425$	$p = .001$
Openness (O) Factor	53.35 (8.84)	52.78 (9.96)	$t_{(86)} = -.280$	$p = .780$
O-Fantasy	56.02 (8.95)	56.95 (9.20)	$T_{(86)} = .481$	$p = .632$
O-Aesthetics	49.24 (12.56)	52.00 (9.84)	$t_{(86)} = 1.130$	$p = .262$
O-Feelings	52.47 (10.82)	48.89 (10.18)	$t_{(86)} = -1.597$	$p = .114$
O-Actions	50.72 (7.52)	51.36 (8.08)	$t_{(86)} = .382$	$p = .704$
O-Ideas	52.77 (9.84)	51.91 (10.47)	$t_{(86)} = -.394$	$p = .694$
O-Values	51.30 (6.39)	48.29 (9.29)	$t_{(86)} = -1.732$	$p = .087$
Agreeableness (A) Factor	46.57 (9.81)	40.33 (10.58)	$t_{(86)} = -2.850$	$p = .005$
A-Trust	52.01 (10.41)	39.71 (12.99)	$t_{(86)} = -4.833$	$p < .001$
A-Straightforwardness	45.74 (7.89)	41.83 (10.63)	$t_{(86)} = -1.922$	$p = .058$
A-Altruism	50.51 (8.59)	42.51 (12.79)	$t_{(82.524)*} = -3.492$	$p = .001$
A-Compliance	44.75 (9.93)	44.56 (9.73)	$t_{(86)} = -.090$	$P = .928$
A-Modesty	44.41 (7.27)	47.13 (7.91)	$t_{(86)} = 1.663$	$p = .100$
A-Tendermindedness	50.38 (10.98)	47.31 (10.58)	$t_{(86)} = -1.334$	$p = .186$
Conscientiousness (C) Factor	46.46 (9.03)	35.69 (9.03)	$t_{(86)} = -5.570$	$p < .001$
C-Competence	48.16 (10.12)	34.93 (9.91)	$t_{(86)} = -6.179$	$p < .001$
C-Order	46.44 (7.81)	45.04 (9.93)	$t_{(86)} = -.724$	$p = .471$
C-Dutifulness	46.53 (5.94)	38.93 (9.05)	$t_{(81.800)*} = -4.730$	$p < .001$
C-Achievement Striving	47.65 (9.63)	40.98 (12.33)	$t_{(86)} = -2.782$	$p = .007$
C-Self-Discipline	42.11 (11.65)	30.32 (10.20)	$t_{(81)} = -5.062$	$p < .001$
C-Deliberation	53.86 (11.17)	46.18 (9.40)	$t_{(81)} = -3.503$	$p = .001$

*df adjusted due to heterogeneity of variance

<u>Psychiatric Diagnostic Screening Questionnaire (PDSQ)</u>

High-SPQs were found to have significantly higher overall PDSQ scores (see Table 17). The percentage of participants meeting criteria for Major Depressive Disorder ($\underline{x}^2$ (1) = 10.476, $\underline{p}$ = .001), Generalized Anxiety Disorder($\underline{x}^2$ (1) = 7.333, $\underline{p}$ = .007), Panic Disorder ($\underline{x}^2$ (1) = 5.366, $\underline{p}$ = .021), Psychosis ($\underline{x}^2$ (1) = 7.333, $\underline{p}$ = .007), Somatization ($\underline{x}^2$ (1) = 5.366, $\underline{p}$ = .021), Obsessive-Compulsive Disorder($\underline{x}^2$ (1) = 11.978, $\underline{p}$ < .001), Social Phobia ($\underline{x}^{22}$ (1) = 18.707, $\underline{p}$ < .001), and Hypochondriasis ($\underline{x}^2$ (1) = 9.402, $\underline{p}$ = .002) was significantly higher among High-SPQs. In contrast, significant group differences were not observed when comparing the percentage of individuals meeting diagnostic criteria for Posttraumatic Stress Disorder, Alcohol Use, Drug Use, Bulimia/Binge Eating, and Agoraphobia.

Table 17. PDSQ Total Scores and Percentage meeting criteria for DSM-IV Diagnostic Categories.

Variable	Ave-SPQ Mean (SD)/% n = 40	High-SPQ Mean (SD)/% n = 48	Statistic	P value
PDSQ Total	9.58 (7.23)	30.02 (16.43)	$t_{(65.419)*} = 7.571$	$p < .001$
PDSQ Total T Score	36.98 (3.44)	46.26 (7.68)	$t_{(65.918)*} = 7.456$	$p < .001$
MDD	0.00%	22.92%	$x^2_{(1)} = 10.476$	$p = .001$
GAD	0.00%	16.67%	$x^2_{(1)} = 7.333$	$p = .007$
PD	0.00%	12.50%	$x^2_{(1)} = 5.366$	$p = .021$
PTSD	0.00%	8.33%	$x^2_{(1)} = 3.492$	$p = .062$
ALC	5.00%	8.33%	$x^2_{(1)} = .382$	$p = .537$
DRG	0.00%	6.25%	$x^2_{(1)} = 2.588$	$p = .108$
PSY	0.00%	16.67%	$x^2_{(1)} = 7.333$	$p =. 007$
BUL/BED	0.00%	4.17%	$x^2_{(1)} = 1.705$	$p <.192$
SOM	0.00%	12.50%	$x^2_{(1)} = 5.366$	$p = .021$
OCD	7.50%	39.58%	$x^2_{(1)} = 11.978$	$p = .001$
SPHO	22.5%	68.75%	$x^2_{(1)} = 18.707$	$p <. 001$
HYPO	0.00%	20.83%	$x^2_{(1)} = 9.402$	$p = .002$
AGOR	2.5%	4.17%	$x^2_{(1)} = .184$	$p = .668$

*df adjusted due to heterogeneity of variance

MDD: Major Depressive Disorder; GAD: Generalized Anxiety Disorder; PD: Panic Disorder; PTSD: Posttraumatic Stress Disorder; ALC: Alcohol Abuse/Dependence; DRG: Drug Abuse/Dependence; PSY: Psychosis; BUL/BED: Bulimia/Binge-Eating Disorder; SOM: Somatization Disorder; OCD: Obsessive Compulsive Disorder; SPHO: Social Phobia; HYPO: Hypochondriasis; AGOR: Agoraphobia.

Action Inhibition Task-Revised data

Response time (RT) tasks

On RT Task #1 High-SPQs (M = 309.197 ms, SD = 91.602 ms) and Ave-SPQs (M = 294.125 ms, SD = 42.38 ms) did not differ in the time taken to lift off the home key after the presentation of the Go stimulus (i.e., the green circle), t (23) = .556, p = .684, d = .21. Within the same task, High-SPQs (M = 494.93 ms, SD = 128.43 ms) and Ave-SPQs (M = 499.510 ms, SD = 67.37 ms) also did not differ in the amount of time taken to reach and depress the response key (i.e., the response time) after the presentation of the Go stimulus, t (4.563) = -.077, p = .942, d = -.04. On RT Task #2, which required participants only to lift off the home key, High-SPQs' (M = 389.47 ms, SD = 171.39 ms) and Ave-SPQs' (309.15 ms, SD = 41.39 ms) HKRT also did not significantly differ, t (4.117) = 1.040, p = .355, d = .31. Taken together these results suggest that across simple RT tasks groups performed similarly on both RTs and HKRTs. Thus, any RT or HKRT differences observed among groups on the AIT-R cannot easily be explained by a discrepant performance in general response speed.

Action Inhibition Task-Revised data

Unless otherwise indicated, the following analyses employed a RM-ANOVA with PREP and CON as the within-subject variables and group (i.e., Ave-SPQ, High-SPQ) as the between-subject variable.

NoGo errors. When examining inhibitory error rates, our task manipulations were found to be successful. First, as anticipated, a main effect of PREP (F [86, 1] = 166.167, p < .001) was observed, with participants making greater NoGo errors on trials of hiPREP (M = .30, SD =.18) than on trials of loPREP (M=.11, SD=.08) (refer to Figure 15). Second, a main effect of CON was also observed (F [86, 1] = 150.844, p < .001), with greater errors observed

on trials in which the perceptual similarity between Go and NoGo signals was highly similar ($\underline{M}$ = .27, SD = .14) relative to trials in which perceptual similarity was low ($\underline{M}$ =.14, SD = .13) (refer to Figure 15). A PREP x CON interaction was also observed ($\underline{F}$ [86, 1] = 10.146, $\underline{p}$ = .002) with participants making disproportionately greater errors on hiPREP, relative to loPREP, trials in conditions of hiCON ($\underline{M}_{hiPREPhiCON}$ = .38, SD = .20, $\underline{M}_{loPREPhiCON}$ = .16, SD = .11; $\underline{t}$ (87) = -13.008, $\underline{p}$ < .001) in comparison to when CON difficulty was low ($\underline{M}_{hiPREPloCON}$ = .21, SD = .20, $\underline{M}_{loPREPloCON}$ = .06, SD = .08; $\underline{t}$ (87) = -7.827, $\underline{p}$ < .001).

Table 18. Group error rates across experimental conditions

Group	PREP difficulty	CON difficulty	Mean (SD)
Ave-SPQs	Low	Low	.08 (.07)
		High	.17 (.10)
	High	Low	.23 (.18)
		High	.43 (.18)
High-SPQs	Low	Low	.04 (.07)
		High	.16 (.14)
	High	Low	.18 (.20)
		High	.32 (.21)
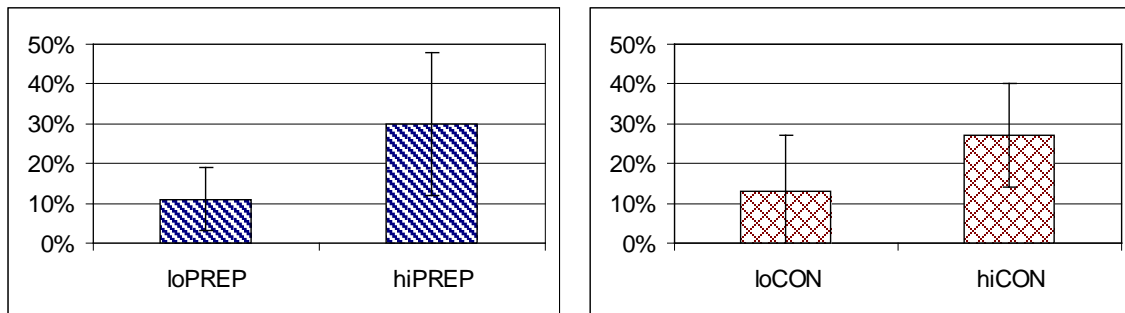
(a)   (b)

Figure 15. NoGo error rates across levels of PREP (a) and CON (b).

When comparing performance across groups, a main effect of group was also observed, $\underline{F}$ (1, 86) = 4.082, $\underline{p}$ = .046. Specifically, High-SPQs made significantly more inhibitory errors

($\underline{M}$=.228, SE=.018) relative to Ave-SPQs ($\underline{M}$=.176, SE=.019). A significant Group x PREP interaction was also found, (F [1, 86] = 4.190, p = .044) revealing that High-SPQs made significantly greater inhibitory errors only in hiPREP conditions ($\underline{M}_{high-spq}$ = .33, $SD_{high-spq}$ = .19; $\underline{M}_{ave-spq}$ = .25, $SD_{ave-spq}$ = .16; $\underline{t}$ [86] = 2.133, $\underline{p}$ = .036) but not in loPREP conditions ($\underline{M}_{high-spq}$ = .12, $SD_{high-spq}$ = .09; $\underline{M}_{ave-spq}$ = .10, $SD_{ave-spq}$ = .07; $\underline{t}$ [86] = 1.398, $\underline{p}$ = .166). Importantly, however, further analyses uncovered a significant Group x PREP x CON interaction ($\underline{F}$ [86, 1], = 5.245, $\underline{p}$ = .024), whereby High-SPQs made disproportionately greater inhibitory errors within hiPREP trials as CON demands increased (i.e., hiPREP, hiCON: $\underline{M}_{high-spq}$ = .43, $SD_{high-spq}$ = .20) relative to AveSPQs ($\underline{M}_{ave-spq}$ = .32, $SD_{ave-spq}$ = .18; $\underline{t}$ [86] = 2.716, $\underline{p}$ = .008) (refer to Figure 16). In contrast, no group difference was observed when comparing NoGo error rates on trials of hiPREP, but loCON ($\underline{M}_{high-spq}$ = .23, $SD_{high-spq}$ = .22; $\underline{M}_{ave-spq}$ = .18, $SD_{ave-spq}$ = .17; $\underline{t}$ [86] = 1.157, $\underline{p}$ = .251). Taken together these results lend partial support for our prediction that High-SPQs would show disproportionate impairment as CON demands increased. Specifically, High-SPQs are, indeed, disproportionately impacted by hiCON demands, but only within hiPREP trials.
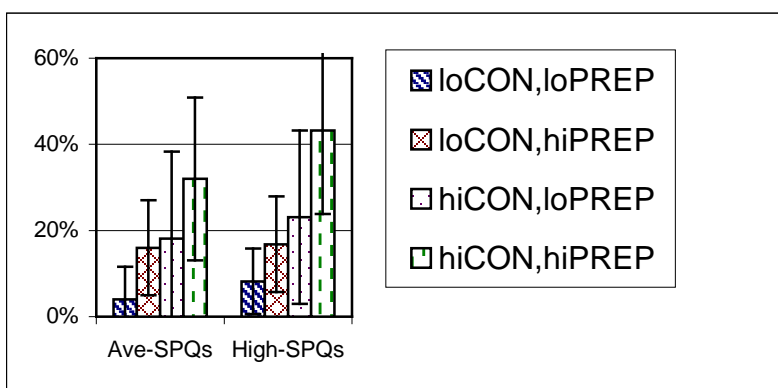
Figure 16. NoGo error rates in Ave-SPQs and High-SPQs across levels of PREP and CON.

Unrelated to the significant Group x PREP interaction was a significant group difference observed across trials of loPREP, loCON ($\underline{M}_{high-spq}$ = .08, $SD_{high-spq}$ = .10; $\underline{M}_{ave-spq}$ = .04, $SD_{ave-spq}$ = .05; $\underline{t}$ [72.694*] = 2.576, $\underline{p}$ = .012. This difference likely reflects a generalized deficit in SCZ rather than a result of difficulty manipulations to PREP and CON.

Go Errors. Errors of omission on Go trials (i.e., Go errors) were also examined. Given the logic motivating the study, we expected that manipulations to PREP and CON difficulty would affect both NoGo *and* Go error rates. Specifically, we argue that individuals with SCZ show deficits on NoGo trials at least in part because of difficulty distinguishing task stimuli denoting Go and NoGo. Logically it follows that increasing the perceptual similarity of task stimuli would also show systematically larger error rates on Go trials. When examining Go errors, a main effect of PREP was observed ($\underline{F}$ [86, 1] = 60.677, $\underline{p}$ < .001) with participants making greater Go errors on loPREP trials ($\underline{M}$=.15, SD=.09) compared to hiPREP trials ($\underline{M}$ = .08, SD =.03). Although increasing the prepotency to respond to a Go trial (via PREP manipulations) increases difficulty in NoGo trials, it logically also decreases the likelihood of Go errors (i.e., errors of omission). Thus, when examining Go errors, the "difficult" PREP condition (80% Go trials) should actually be viewed as the less difficult Go PREP condition. This finding provides further confirmation of the effectiveness of our PREP manipulation. A main effect of CON was also observed ($\underline{F}$ [86, 1] = 59.511, $\underline{p}$ < .001) with greater Go error rates observed in trials of hiCON ($\underline{M}$ = .13, SD = .07) relative to loCON ($\underline{M}$ = .09, SD = .05). This finding confirms our prediction that increasing perceptual similarity of Go and NoGo stimuli would increase Go error rates.

A PREP x CON interaction was also observed ($\underline{F}$ [86, 1] = 21.757, $\underline{p}$ < .001), revealing that participants made disproportionately greater errors as CON demands increased within

trials in which demands to respond to the prepotent response (i.e., to Go) were lower ($\underline{M}$=.178, SD = .11) rather than higher ($\underline{M}$ = .09, SD = .03). After accounting for the opposing effects of PREP manipulations within Go and NoGo trials, these results confirm those found when examining NoGo errors. More succinctly, the CON manipulation was most effective, across both Go and NoGo trials, in conditions in which the PREP manipulation served to increase the likelihood of making an error. A main effect of Group was also observed, ($\underline{F}$ [1, 86] = 5.637, $\underline{p}$ = .020), with High-SPQs making significantly more Go errors ($\underline{M}$ = .12, SE = .06) than AveSPQs ($\underline{M}$ = .10, SD = .03). Importantly, the fact that High-SPQs show greater error rates among both NoGo *and* Go trials provides indirect support for our contention that errors observed on tasks of action inhibition within High-SPQs are mediated by factors other than PREP difficulty. Specifically, if task performance (including error rates) were primarily mediated by PREP demands, we would expect High-SPQs, relative to Ave-SPQs, to have greater error rates on NoGo trials but fewer error rates on Go trials due to the increased prepotency to depress the home key, regardless of whether it was a NoGo or Go trial. This finding, is tempered, however, by the significant PREP x Group interaction ($\underline{F}$ [1, 86] = 6.579, $\underline{p}$ = .012), which indicates that High-SPQs had higher Go error rates on conditions of loPREP (i.e., blocks including 50% Go trials; $\underline{M}_{high\text{-}spq}$ = .17, SD$_{high\text{-}spq}$ = .11; $\underline{M}_{ave\text{-}spq}$ = .12, SD$_{ave\text{-}spq}$ = .05; $\underline{t}$ [68.338*] = 2.684, $\underline{p}$ = .009) but not hiPREP (i.e., blocks including 80% Go; $\underline{M}_{high\text{-}spq}$ = .08, SD$_{high\text{-}spq}$ = .03; $\underline{M}_{ave\text{-}spq}$ = .08, SD$_{ave\text{-}spq}$ = .02; $\underline{t}$ [86] = .956, $\underline{p}$ = .342) (refer to Figure 17). In contrast to the observations above, this finding argues that PREP demands are associated with task difficulty to a greater extent within High-SPQs than Ave-SPQs. That is, High-SPQs' error rates in Go trials are disproportionately greater, relative to Ave-SPQs, when the prepotency to depress the home key is less (i.e., loPREP). Thus, the main effect of Group

appears to be accounted for by disproportionately high error rates in conditions of loPREP. A

Group x CON interaction was <u>not</u> observed, ($\underline{F}$ [1, 86] = 1.462, $\underline{p}$ = .230) suggesting that

groups were equally effected by increasing CON demands. There was also no Group x PREP

x CON interaction observed, $\underline{F}$ [1, 86] = .735, $\underline{p}$ = .394.

Table 19. Group Go error rates across experimental condition

Group	PREP difficulty	CON difficulty	<u>M</u>	SD
Ave-SPQs	Low	Low	.08	.09
		High	.16	.11
	High	Low	.07	.03
		High	.09	.03
High-SPQs	Low	Low	.14	.09
		High	.20	.11
	High	Low	.07	.03
		High	.09	.03
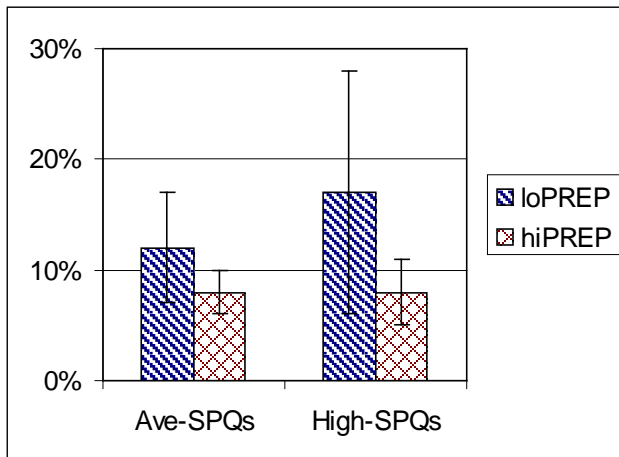
Figure 17. Go error rates in Ave-SPQs and High-SPQs across levels of PREP difficulty.

GoRT trials. A main effect of PREP was observed, ($\underline{F}$ [1, 85] = 85.845, $\underline{p}$ < .001), with

participants responding significantly faster on Go trials in which PREP demands were low (i.e.,

80% of trials were Go trials; $\underline{M}$ = 1134.95 ms, SD = 110.57 ms) compared to when PREP

demands were high (i.e., 50% of trials were Go trials; $\underline{M}$ = 1059.34 ms, SD = 121.18 ms). A

main effect of CON was also observed, ($\underline{F}$ [1, 85] = 24.086, $\underline{p}$ < .001), indicating that

participants responded significantly faster when the perceptual similarity of Go and NoGo

stimuli was lower ($\underline{M}$ = 1077.53 ms, SD = 105.63 ms) compared to higher ($\underline{M}$ = 1115.27 ms,

SD = 124.82 ms). No PREP x CON interaction was observed, $\underline{F}$ (1, 85) = 2.261, $\underline{p}$ = .136.

Overall, groups did not differ in their GoRTs, $\underline{F}$ (1, 85) = .304, p = .583 ($\underline{M}_{high\text{-}SPQ}$ =

1090.608 ms, $SD_{high\text{-}SPQ}$ = 131.56 ms; $\underline{M}_{ave\text{-}SPQ}$ = 1103.68 ms, $SD_{ave\text{-}SPQ}$ = 77.52 ms). In

addition, PREP difficulty was not found to differentially impact GoRTs across groups as

evidenced by the absence of a Group x PREP interaction, $\underline{F}$ (1, 85) = 1.300, $\underline{p}$ = .257. There

was, however, a Group x CON interaction found, ($\underline{F}$ [1. 85] = 4.682, $\underline{p}$ = .033, showing Ave-

SPQs to have significantly longer GoRTs on trials of hiCON ($\underline{M}_{high\text{-}SPQ}$ = 1101.42 ms, $SD_{high\text{-}}$

$_{SPQ}$ = 149.81 ms; $\underline{M}_{ave\text{-}SPQ}$ = 1131.54 ms, $SD_{ave\text{-}SPQ}$ = 85.54 ms) but not loCON ($\underline{M}_{high\text{-}SPQ}$ =

1078.96 ms, $SD_{high\text{-}SPQ}$ = 120.50 ms; $\underline{M}_{ave\text{-}SPQ}$ = 1075.82 ms, $SD_{ave\text{-}SPQ}$ = 85.93 ms) (refer to

Figure 18). This finding suggests that groups are differentially impacted by increases in CON

difficulty. While Ave-SPQs slow their RTs as CON increases, High-SPQs, as indexed by their

RTs, are relatively impervious to CON manipulations. A Group x PREP x CON interaction

was not observed, $\underline{F}$ (1, 85) = 2.261, $\underline{p}$ = .136. These findings confirm results of Study 1 in

which increases in CON resulted in decreased SURT among Ave-SPQs but not High-SPQs.

Mean group GoRTs across experimental conditions are reported in Table 20.

Table 20. Group GoRTs (in msec) across experimental conditions

Group	PREP difficulty	CON difficulty	Mean (SD)
Ave-SPQs	Low	Low	1116 (107)
		High	1156 (133)
	High	Low	1034 (126)
		High	1106 (133)
High-SPQs	Low	Low	1119 (110)
		High	1147 (137)
	High	Low	1041 (130)
		High	1056 (137)
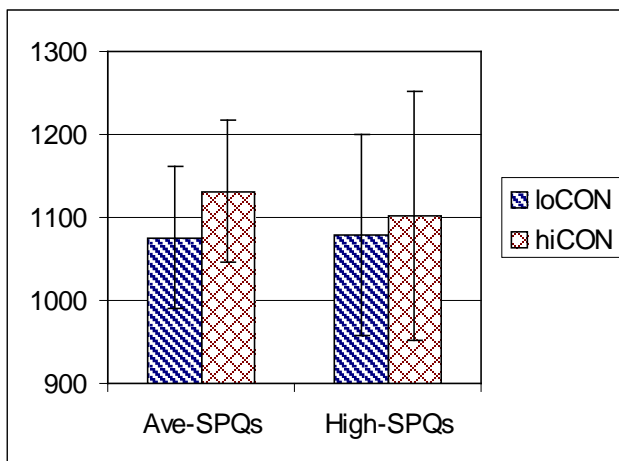
Figure 18. GoRTs of Ave-SPQs and High-SPQs across levels of CON difficulty

HKRT. To test the impact of PREP and CON manipulations at early stages of movement, HKRT, was examined. Analyses were divided into Go and NoGo trials and restricted to only correct trials.

HKRT on Go trials (GoHKRT). A main effect of PREP, $\underline{F}$ (1, 85) = 83.078, $\underline{p} < .001$, was found, with participants making significantly slower GoHKRT in conditions of loPREP ($\underline{M}$ = 857.53 ms, SD = 111.85 ms) relative to hiPREP ($\underline{M}$ = 768.73 ms, SD = 120.67 ms). A main effect of CON was also observed ($\underline{F}$ [1, 85] = 5.158, $\underline{p}$ = .026) with participants making

significantly longer GoHKRT on trials of hiCON (M = 825.10 ms, SD = 130.32 ms) compared

to loCON (M = 801.92 ms, SD = 103.85 ms). A PREP x CON interaction was *not* observed, F

(1, 85) = 1.793, p = .184.

A trend towards a significant main effect of Group was found (F [1, 85] = 3.453, p =

.067), indicating that High-SPQs (M = 794.64 ms, SD = 131.31 ms) lifted off the HK

marginally faster than Ave-SPQs (M = 836.96, SD = 63.97 ms). Further analysis indicated a

trend towards a significant Group x CON interaction (F [1, 85] = 3.011, p = .086) with Ave-

SPQs having significantly slower HKRT during trials of hiCON ($M_{high\text{-}spq}$ = 797.41 ms , $SD_{high\text{-}spq}$ = 157.64 ms; $M_{ave\text{-}spq}$ = 857.64 ms, $SD_{ave\text{-}spq}$ = 78.92 ms) but not loCON ($M_{high\text{-}spq}$ = 789.95

ms, $SD_{high\text{-}spq}$ = 120.34 ms; $M_{ave\text{-}spq}$ = 816.28 ms, $SD_{ave\text{-}spq}$ = 78.86 ms) (Figure 19). These

results provide additional evidence that the task performance of Ave-SPQs, but not High-

SPQs, is impacted by increasing levels of CON difficulty. Groups were not found to be

differentially impacted by manipulations of PREP (F [1, 85] = .953, p = .332). A Group x

PREP x CON (F [1, 85] = 1.481, p = .227) interaction was also not observed. Groups' mean

GoHKRTs across experimental conditions is reported in Table 22.

Table 21. Groups' mean GoHKRTs (in msec) across experimental condition

Group	PREP difficulty	CON difficulty	Mean (SD)
Ave-SPQs	Low	Low	866 (101)
		High	884 (158)
	High	Low	766 (139)
		High	830 (127)
High-SPQs	Low	Low	840 (103)
		High	844 (158)
	High	Low	743 (137)
		High	750 (123)
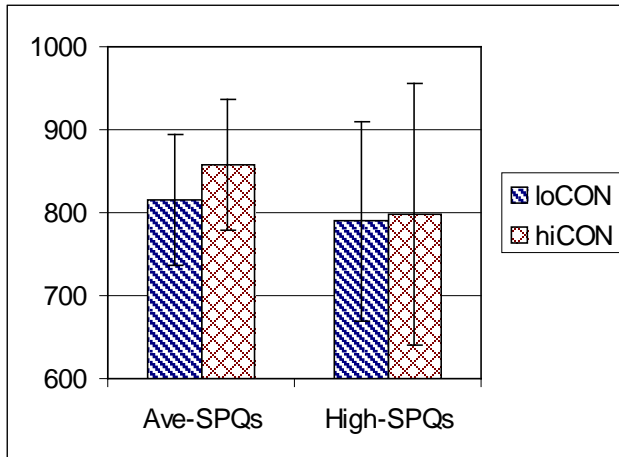
Figure 19. Ave-SPQs and High-SPQs' GoHKRTs (in msec) across levels of CON difficulty

HKRT on NoGo trials (NoGoHKRT). Results from Study 1 suggested that HKRT may serve as an early proxy for AI. To more fully explore this possibility, participants in Study 2 were explicitly instructed to keep their hand on the home key button on NoGo trials. In providing this instruction, any NoGoHKRT is more likely to reflect an early marker of the failure to inhibit a prepotent response. Analysis revealed a main effect of PREP ($\underline{F}$ [1, 83] = 59.508, $\underline{p}$ < .001), with participants releasing from the home key faster on trials of hiPREP ($\underline{M}$ = 808.79 ms, SD = 89.76 ms) than loPREP ($\underline{M}$ = 868.46 ms, SD = 80.58 ms). A main effect of CON ($\underline{F}$ [1, 83] = 15.080, $\underline{p}$ < .001) was also observed, indicating that participants had faster NoGoHKRTs on trials of loCON ($\underline{M}$ = 819.83 ms, SD = 76.01 ms) than hiCON ($\underline{M}$ = 855.21 ms, SD = 97.17 ms) (Figure). No PREP x CON interaction was observed, $\underline{F}$ (1, 83) = .748, $\underline{p}$ = .390.

No group differences were observed in overall HKRTs, $\underline{F}$ (1, 83) = .983, $\underline{p}$ = .324. As anticipated, groups were also not observed to be disproportionately impacted by manipulations of PREP ($\underline{F}$ [1, 83] = .100, $\underline{p}$ = .753). Unexpectedly, a Group x CON interaction was not observed, $\underline{F}$ [1, 83] = .104, $\underline{p}$ = .748. A Group x PREP x CON interaction ($\underline{F}$ [1, 83] = 2.165, $\underline{p}$

128

= .145) was also not observed. The fact that High-SPQs were not disproportionately impacted

by increasing levels of CON difficulty initially appears inconsistent with findings from Study 1

in which CON difficulty differentially impacted groups' HKRTs in both SU and INH

conditions. This difference may reflect differences in movement planning and/or execution

requirements across tasks. For example, across all trials in the AIT (i.e., Go, SU, or INH),

participants are initially presented with a green circle which invariably signals a Go response.

Thus, in a sense SU HKRTs and INH HKRTs can both be viewed as forms of Go HKRTs

(within the context of a modulatory signal), potentially accounting for similar group

performance across SU and INH trials. In contrast, within the AIT-R (Study 2), inhibitory

trials (i.e., NoGo) do not require participants to lift off the home key to initiate a "Go response

(i.e., no green circle is presented).

Table 22. Group HKRTs (in msec) on NoGo trials across experimental conditions

Group	PREP difficulty	CON difficulty	Mean (SD)
Ave-SPQs	Low	Low	860 (87)
		High	894 (100)
	High	Low	794 (87)
		High	837 (119)
High-SPQs	Low	Low	839 (88)
		High	889 (102)
	High	Low	789 (88)
		High	804 (122)

Relationship between experimental task data and clinical measures

Experimental variables from the AIT-R correlated significantly with various clinical

measures across the various clinical measures, particularly within the Schizotypal Personality

Questionnaire (SPQ).   A detailed list of all significant correlations is reported in Appendix W.

The Cognitive-Perceptual factor of the SPQ correlated with NoGo error rates in the loPREP-loCON, hiPREP-loCON, and hiPREP,hiCON conditions as well as error rates in the Go error rates in the loPREP-loCON and hiPREP-loCON conditions. The Cognitive-Perceptual factor score also correlated with GoRTs in the hiPREP, hiCON condition as well as GoHKRTs in hiPREP, loCON and hiPREP, hiCON conditions. Interpersonal factor scores of the SPQ correlated with GoHKRTs in hiPREP, hiCON condition. Go error rates in the loPREP,loCON and hiPREP,hiCON conditions as well as NoGoHKRTs in hiPREP, hiCON trials. Scores on SPQ's Disorganized factor correlated with GoHKRTs in the hiPREP, hiCON condition.

The Ideas of Reference subscale of the SPQ correlated positively with NoGo error rates in the hiPREP-loCON and hiPREP-hiCON conditions, GoRTs in the hiPREP, hiCON condition, and GoHKRTs in the hiPREP, hiCON condition. The Odd Speech subscale correlated with GoHKRTs in hiPREP, hiCON while the Suspiciousness subscale negatively correlated with GoHKRTs in hiPREP, loCON and hiPREP, hiCON trials. Excessive Social Anxiety correlated positively with Go error rates in the hiPREP, hiCON condition as well as GoHKRTs on hiPREP, hiCON trials.

Unusual Perceptual Experiences correlated with GoHKRTs in the hiPREP, hiCON condition. Odd/Eccentric Behaviour scores correlated with GoHKRTs in hiPREP, hiCON conditions. Odd Beliefs/Magical Thinking correlated positively with NoGo error rates in the loPREP-loCON, hiPREP, loCON, and hiPREP, hiCON conditions. Odd Beliefs/ Magical Thinking correlated positively with Go error rates in the loPREP-loCON, hiPREP-loCON conditions as well as GoRTs in loPREP, loCON and GoRTs in hiPREP, loCON conditions. No Close Friends subscale score correlated with GoHKRTs in hiPREP, hiCON and NoGoHKRTs in the hiPREP, hiCON condition. Constricted Affect correlated with NoGo error

rates in the loPREP-loCON condition. Suspiciousness correlated with loPREP, loCON, loPREP, hiCON, hiPREP, loCON, and hiPREP, hiCON NoGo error rates.

Fewer significant correlations were observed when comparing experimental variables to the PAI. The Antisocial scale of the PAI correlated with NoGo error rates in hiPREP-hiCON trials, the Alcohol Problems correlated with Go error rates in the loPREP-loCON condition, and the Anxiety-Related Disorders scale score correlated with GoRTs within loPREP, loCON conditions.

When comparing AIT-R performance with scores on the NEO-PI-R, Extroversion factor scores correlated with GoRTs in the hiPREP, loCON condition. The Agreeableness factor score correlated negatively with NoGo error rates in the loPREP-loCON condition. The Conscientiousness factor score correlated negatively with GoHKRTs in the hiPREP, hiCON condition. Estimations of FSIQ correlated, in the negative direction, with Go errors in the loPREP-hiCON condition, and negatively with NoGo errors in the loPREPloCON and hiPREPhiCON conditions. Various facet scores (within domains of Neuroticism, Extraversion, Openness to Experience, Agreeableness, and Conscientiousness) were also found to correlate significantly with select AIT-R experimental variables (see Appendix W).

COMT genotyping

To assess whether High-SPQs and Ave-SPQs had discrepant frequency distributions of COMT bi-allelic variants, a Chi Square test was conducted with Group (i.e., High-SPQ, Ave-SPQ) and COMT genotype (i.e., val/val, val/met, met/met) as variables. We did not observe a significant relationship between Group and COMT genotype, χ^2 (2) = 1.448, $\underline{p}$ = .485. Participants' COMT genotypes, categorized by Group, are reported in Table 23.

Table 23. Frequency distributions of COMT genotypes across Ave-SPQ and High-SPQ

	Ave-SPQ	High-SPQ
val/val	24.1%	36.4%
val/met	20.7%	13.6%
met/met	55.2%	50.0%

Given that COMT bi-allelic variation did not differ as a function of group, statistical analyses were conducted on data collapsed across groups. Unless otherwise indicated, the following analyses employed a RM-ANOVA with PREP and CON as within-subject variables and COMT (i.e., val/val, val/met, met/met) as the between-subject variable. Main effects of PREP and CON are reported above (when discussing RM-ANOVA results with regards to High-SPQs and Ave-SPQs). Thus, for the sake of concision, the following review of statistical results will focus on differences observed across COMT genotypes (i.e., main effects of COMT genotype as well as significant COMT interactions: COMT x PREP, COMT x CON, and COMT x PREP x CON interactions).

NoGo errors. No main effect of COMT, $\underline{F}$ (70, 2) = .819, $\underline{p}$ = .445, was found, with val/vals ($\underline{M}$ = .180, SD = .10), val/mets ($\underline{M}$ = .219, SD = .127), and met/mets ($\underline{M}$ = .23, SD = 173) showing comparable error rates on NoGo trials (i.e., inhibitory trials). No COMT x PREP ($\underline{F}$ [70,2] = .427, $\underline{p}$ = .654), no COMT x CON interaction ($\underline{F}$ [70, 2] = .476, $\underline{p}$ = .623), or COMT x PREP x CON, ($\underline{F}$ [70, 2] = 1.087, $\underline{p}$ = .343.

Go errors. No main effect of COMT was observed, indicating that errors of omission on Go trials (i.e., Go errors) did not significantly differ across val/val ($\underline{M}$ = .111, SD = 079), val/met ($\underline{M}$ = .117, SD = .042), and met/met ($\underline{M}$ = .107, SD = .046) genotypes, $\underline{F}$ (70, 2) = .162, $\underline{p}$ = .851. COMT x PREP ($\underline{F}$ [70, 2] = .160, $\underline{p}$ = .852), COMT x CON ($\underline{F}$ [70, 20] = .037, $\underline{p}$ =

.963), or COMT x PREP x CON (F [70, 2] = .189, p = .828) interactions were also not observed.

   GoRTs. A trend towards a main effect of COMT, (F [70,2] = 2.255, p = .113 with val/vals (M = 1132.74 ms, SD = 80.40 ms) observed to have longer response times than met/mets (M = 1051.54 ms, SD = 160.40 ms), p = .046. GoRTs in val/vals and met/vals (M = 1087.96 ms, SD = 108.40 ms) were not found to be significantly different, p = .138. A significant group difference was also not observed between met/vals and met/mets, p = .326. COMT x PREP (F [70, 2] = 2.111, p = .129), COMT x CON, (F [70, 2] = .597, p = .553), or COMT x PREP x CON, (F [70, 2] = .899, p = .412) interactions were not observed.

   NoGoHKRTs. No main effect of COMT, F (2, 67) = .212, p = .809 was observed, with met/vals (M = 831.39 ms, SD = 70.51 ms), met/mets (M = 841.43 ms, SD = 111.81 ms), and val/vals (M = 844.47 ms, SD = 68.27 ms) found to have comparable HKRT on correct NoGo trials. Neither COMT x PREP (F [2, 67] = .356, p = .702) nor COMT x CON (F [2, 67] = .143, p = .867) interactions were observed. However, there was a trend towards a significant COMT x PREP x CON interaction, F (2, 67) = 2.557, p = .085. Simple effects testing, however, did not reveal any group differences across any of the 4 experimental conditions (e.g., loPREP-loCON, loPREP-hiCON, hiPREP-loCON, hiPREP-hi-CON).

   GoHKRTs. No main effect of COMT was observed, F (69, 2) = .854, p = .430, indicating that Val/Mets (M = 804.83 ms, SD = 107.09 ms), met/mets (M = 780.88 ms, SD = 166.42), and val/vals (M = 832.61 ms, SD = 91.56 ms) did not have significantly different GoHKRTs. COMT x PREP (F [2, 69] = .595, p = .554), COMT x CON, (F [2, 69] = .049, p = .952), and COMT x PREP x CON interactions was also not observed, F (2, 69) = .946, p = .393.

Relationship between COMT genotype and clinical measures

Correlational analyses were conducted for the entire sample between error rates (Go and NoGo) and various clinical measures. Results, organized by clinical measure, are reported below.

Personality Assessment Inventory

Positive Impression Management (PIM) scores were found to significantly vary across groups, F (2, 66) = 4.032, p = .022, with met/mets (M = 53.18, SD = 6.78) having significantly higher PIM T scores than both val/vals (M = 45.65, SD = 10.45; p = .043) and met/vals (M = 43.65, SD = 10.09; p = .006). Drug Use, as indexed by the PAI clinical scale, was also found to vary as a function of COMT genotype, F (2, 66) = 3.659, p = .031. Specifically, met/mets (M = 54.75, SD = 8.80) had significantly higher T scores on this measure relative to met/vals (M = 49.49, SD = 6.30; p = .031) as well as val/vals (M = 6.98, SD = 1.52; p = .010).

Schizotypal Personality Questionnaire

No significant associations were found between COMT genotype and any of the SPQ factor scores (i.e., Interpersonal, Cognitive-Perceptual, Disorganized) or nine subscales (i.e., ideas of reference, excessive social anxiety, odd beliefs/magical thinking, unusual perceptual experiences, odd eccentric beliefs, no close friends, odd speech, constricted affect, and suspiciousness).

NEO-Personality Inventory-Revised (NEO-PI-R)

NEO-PI-R Factor scores (i.e., Neuroticism, Extraversion, Openness to Experience, Agreeableness, and Conscientiousness) did not vary as a function of COMT genotype. There was, however, a significant relationship found between T scores on the facet E-Gregariousness and COMT genotype, F (2, 70) = 2.875, p = .063. Post-hoc analysis revealed that met/mets (M

= 42.99, SD = 13.67) had significantly lower scores on Gregariousness than met/vals ($\underline{M}$ = 53.47, SD = 12.01; $\underline{p}$ = .019) but not val/vals ($\underline{M}$ = 50.62, SD = 14.80; $\underline{p}$ = .109). Met/vals and val/vals did not significantly differ on this measure ($\underline{p}$ = .418). No other significant relationships between COMT and NEO-PI-R facet scores were also observed.

Psychiatric Diagnostic Screening Questionnaire

The proportion of individuals meeting diagnostic criteria for DSM disorders, according to PDSQ scores, did not differ as a function of participants' COMT genotype.

WAIS-III

Estimated FSIQ was not found to vary significantly across COMT genotype groups.

Discussion

The current experiment utilized a novel Go/NoGo paradigm in order to examine the impact of systematic increases in PREP and CON demands across groups of High-SPQ and Ave-SPQ participants. This study sought to test the hypothesis that schizotypy is related to disproportionate performance decrements as a function of increased CON demands but relatively intact performance in relation to increased PREP demands.

Action Inhibition Task-Revised

The AIT-R was successful in manipulating PREP and CON demands independently. For instance, greater Go and NoGo errors were observed on trials in which CON was high compared to low. With regards to PREP manipulations, NoGo error rates were higher when PREP difficulty was comparatively high. PREP manipulations also impacted Go error rates. Specifically, by increasing one's prepotency to respond to the Go signal, hiPREP elicited lower Go errors (i.e., failure to respond on a Go trial). Across Go and NoGo trials, participants made disproportionately greater errors in hiCON conditions in which the degree of prepotency most interfered with correct performance (e.g., higher NoGo error rates were elicited in the hiPREP condition while higher Go errors were elicited in the loPREP condition).

Participants' GoRTs were also found to be impacted by PREP and CON manipulations. Specifically, participants were slower in responding to trials of loPREP (i.e., within blocks where Go trials accounted for 50%, as opposed to 80% of trials). Participants were also observed to have slower GoRTs in conditions in which the perceptual similarity of Go and NoGo stimuli were high (i.e., hiCON). Participants' slowed RTs in response to increased CON is interpreted as a compensatory strategy which enables them to more ably manage increased CON, and perform well on the task. These manipulations elicited a similar pattern of results at

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an earlier stage of movement response – that is, when releasing from the home key. Finding an effect of CON at this early stage in movement responding/planning suggests that CON is able to influence movement in early stages, not just after a response has been initiated.

In addition to the AIT-R, participants completed *simple RT tasks* in order to gauge the potential impact of RT *per se* within the more cognitively challenging AIT-R. In these RT tasks participants were required to make an imperative response to a single stimulus (the word Go) on each trial. Of note, no group differences were found on these measures, indicating that groups did not differ in their ability to respond to easily decipherable Go stimuli in the absence of NoGo stimuli, when required to release the home key *then* depress the response key (RT#1) or simply release from the home key (RT#2). Consequently, group differences observed on the AIT-R were not interpreted as reflecting general response slowness.

Comparison of groups' performance on the AIT-R

High-SPQs were observed to have more errors across both NoGo and Go trials. When examining the pattern of NoGo errors more closely, it was found that High-SPQs made disproportionately more errors in hiPREP trials in which CON demands were also high (e.g., 80% of trials were Go trials:NoGo gap ratio = 8%:6%), compared to when CON demands were low (Go:NoGo gap ratio = 10%:6%). This finding was interpreted as providing partial evidence to support our hypothesis that High-SPQs would be differentially impacted by increases in CON, but not PREP demands. Although this effect was found within a condition in which PREP difficulty was also high, we have interpreted it within the broader context within which High-SPQs were shown to be differentially impacted by increasing CON demands. Thus, we feel comfortable interpreting these results in such a manner.

Unexpectedly, High-SPQs had similar error rates across the other experimental conditions (e.g., loPREP/loCON, loPREP/hiCON, hiPREP/loCON). A potential explanation for comparable error rates across these trials is the 43 cm distance between the home key and response key, within which participants can correct/withdraw their response on inhibition trials. This apparatus layout differs from many other studies using Go/NoGo paradigms in which participants' hands rest directly on the response key throughout the task. Among Go errors, High-SPQs were found to have significantly greater errors only when the prepotency to respond was low. No differential effect of CON was observed between groups on errors of omission (i.e., Go errors).

Overall, GoRTs did not significantly differ between Ave-SPQs and High-SPQs. PREP manipulations also did not differentially affect group RTs. However, groups were found to be differentially impacted by CON demands, with Ave-SPQs showing slower GoRTs on trials of hiCON, but not loCON. Consistent with the pattern of SURT findings from Study 1, the current findings suggest that Ave-SPQs, but not High-SPQs, slow their responding under hiCON conditions, perhaps as a compensatory strategy. These findings are also similar to previous findings showing that individuals with SCZ fail to decrease their RTs in response to increased CON. For example, Kerns et al. (2005) found that during the course of performing the Stroop task individuals with SCZ fail to reduce their RTs after trials of conflict or error. Similarly, Carter et al. (2001) found that SCZ patients fail to significantly reduce their RTs after errors of omission on a degraded version of the AX-CPT task. Notably, this version of the AX-CPT is a task of AI in which CON demands are intentionally taxed by degrading the decipherability of task stimuli.

Functional imaging studies have shown that among healthy participants, the ACC is particularly sensitive to manipulations that alter the decipherability of inhibitory stimuli (Kok, 1986). Kok (1986) found reduced scalp activity over areas indicative of ACC activation. Using fMRI, Kerns et al. (2004) has shown an association between ACC activation and increased conflict with the Stroop task. Specifically, increased ACC activation was observed on trials involving conflict (e.g., reading the color of the word instead of the word itself). ACC activation also predicted adjustments in behaviour on the trials directly following conflict trials (i.e., RTs were slower on congruent trials preceded by incongruent trials vs. congruent trial that were preceded by congruent trials). Our findings, taken together with studies showing the ACC's involvement in CON, are congruent with recent theories of ACC functioning. In the Conflict Monitoring hypothesis, for example, Botvinick et al. (2001) postulate that the ACC serves to monitor for the occurrence of conflicts in information processing.

Groups were also found to be differentially impacted by CON manipulations when examining GoHKRTs, with higher CON demands resulting in slower times among Ave-SPQs, but not High-SPQs. In contrast, NoGoHKRTs were less straightforward. No group differences were observed in overall HKRT. Groups were also not observed to be disproportionately impacted by manipulations of PREP or, unexpectedly, CON. These findings suggest that High-SPQs have less difficulty detecting and deciphering task stimuli when presented before the initiation of movement – e.g., such as during correctly inhibited NoGo trials.

The fact that High-SPQs' NoGoHKRTs were not disproportionately impacted by increasing levels of CON difficulty initially appears inconsistent with findings from Study 1 in which CON difficulty differentially impacted groups' HKRTs in both SU and INH conditions.

This difference may reflect differences in movement planning and/or execution requirements across tasks. For example, across all trials in the AIT (i.e., Go, SU, or INH), participants are initially presented with a green circle which invariably signals a Go response. Thus, in a sense, SUHKRTs and INHHKRTs can both be viewed as forms of GoHKRTs (within the context of a modulatory signal), potentially accounting for similar group performance across SU and INH trials. In contrast, within the AIT-R (Study 2), inhibitory trials (i.e., NoGo) do not require participants to lift off the home key to initiate a Go response (i.e., no green circle is presented).

To use nomenclature recently introduced by Schacher, Logan, Robaey, Chen, Ickowicz, and Barr (2007), the AIT requires action cancellation, while AIT-R requires action restraint. Action restraint is the ability to withhold a strong response tendency of a preplanned action (e.g., Go/NoGo tasks). In comparison, action cancellation requires participants to cancel an ongoing preplanned action (e.g., SSP) (Schacher et al., 2007). Lending support to the existence of unique underlying inhibitory control mechanisms within these tasks is mounting neuropharmacological and neuroanatomical evidence suggesting that these forms of AI are also dissociable at a neuroanatomical and neuropharmacological level (see Eagle, Bari & Robbins, 2008, for review). These findings, taken together, may suggest that High-SPQs' inhibitory HKRT are differentially impacted by increasing CON demands, relative to Ave-SPQs, only on tasks of action-cancellation, but not tasks of action-restraint.

Clinical measures

High-SPQs also scored significantly higher on their total SPQ, factor and subscale scores, relative to Ave-SPQs. High-SPQs demonstrated significantly higher scores on several indices of the PAI including negative impression management, Somatization, Anxiety, Anxiety-Related Disorders, Depression, Mania, Paranoia, Schizophrenia, Borderline,

Antisocial, Alcohol, Suicide, and Nonsupport, but lower on indices of PIM, Treatment Resistance, Dominance, and Warmth. These findings are largely consistent with those reported in Study 1 with one exception. Specifically, the Aggression subscale on the PAI was found to be significantly higher among High-SPQs within study 1 but not study 2. They also provide further evidence to support previous findings of elevated levels of psychopathology within individuals with SPD (Fenton et al., 1997).

With regard to the big five Factor scores, High-SPQs obtained higher scores on Neuroticism but significantly lower scores on the Extroversion, Agreeableness, and Conscientiousness Factors. A group difference was not observed on the Openness to Experience Factor. This five-factor pattern of findings reflects the factor distribution observed in Study 1 as well as in previously documented investigations (Blais, 1997; Trull, 1992; Yeung et al., 1993).

Significant correlations were observed between AIT-R experimental variables (NoGo errors, Go errors, GoRT, GoHKRT, NoGoHKRT) and various clinical measures. Numerous SPQ Factor and Subscale scores correlated significantly with NoGo error rates in the AIT-#2 (e.g., Cognitive-Perceptual Factor, Interpersonal Factors, Ideas of Reference, Excessive Social Anxiety, Odd Beliefs/Magical Thinking, Constricted Affect, and Suspiciousness). Go errors were also found to correlate with the Cognitive-Perceptual Factor score and the Odd Beliefs/Magical Thinking subscale score. SPQ Factor and subscale scores were also found to correlated with GoRT, GoHKRTs, and NoGoHKRTs across certain experimental conditions. Very few subscales of the Personality Assessment Inventory – short form. The Extraversion, Openness to Experience, Agreeableness, and Conscienctiousness factor scores (as well as various facet scores across all five domains) of the NEO-PI-R were also found to correlate with

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certain AIT-R variables. Estimations of FSIQ correlated significantly, in the negative direction, with Go errors in the loPREP-hiCON condition and negatively with NoGo errors in the loPREPloCON and hiPREPhiCON conditions (for further details, see Appendix W).

Collectively these findings suggest that underlying personality features are associated with performance on the AIT-R. Of particular interest is the relationship observed between SPQ scores (factor and subscale) and behavioural indices on the AIT-R. Further investigations, testing specific theoretically-driven hypotheses will be helpful in clarifying how personality architecture contributes to performance in response to increased PREP and CON demands within AI tasks.

COMT

Unexpectedly, no group differences were found when analyzing COMT genotypes in the current sample. Accordingly, High-SPQs and Ave-SPQs were amalgamated in order to form one larger sample for the purpose of analyzing the effect of genotype on task performance. Differential error rates across COMT genotype were not observed when examining NoGo or Go errors. Generally, participants' COMT genotypes impacted very little on measures of GoRT and HKRT. Individuals with the val/val genotype were observed to have marginally longer response times than met/mets, but this effect was restricted to trials in which both PREP and CON demands were low. Although the failure to show associations between COMT and SCZ symptomatology is inconsistent with studies identifying the preferential transmission of the high activity val allele to SCZ offspring has been observed by some (Egan et al., 2001; Li, Sham, Vallada, et al., 1996; Kunugi et al., 1997; Li et al., 2000), they echo the efforts of others who have failed (Karayiorgou et al., 1998; Strous et al., 1997; Wei & Hemmings, 1999).

COMT genotype was also not found to significantly impact participants' performance on the AIT-R, including error rates, RTs, and HKRTs in response to increasing PREP and CON demands. These findings add to the largely inconsistent literature examining the relationship between COMT genotype and cognition found among individuals with SCZ as well as HCs. For instance, the val allele has been found to be associated with poorer performance on prefrontally-mediated cognitive tasks among individuals with SCZ, such as executive functioning, processing speed, and attention (Egan et al., 2001; Malhotra et al., 2002; Weinberger et al., 2001; Bilder et al., 2002; Goldberg et al., 2003; Han et al., 2006). Our findings are, however, consistent with other unsuccessful attempts to show associations between COMT and cognitive functioning (for review, Glatt et al., 2003).

Limitations and future directions

The major disappointment of the current study was the failure of AIT-R to clearly show disproportionate error rates between Ave-SPQs and High-SPQs as CON demands increased, despite differential patterns of GoRTs and GoHKRTs. Although High-SPQs were evidenced to have greater inhibitory errors on trials of hiPREP, hiCON, this finding does not conclusively suggest that CON demands underlie these errors among High-SPQs. As discussed above, this finding may be related to the unusually long distance between the home key and response key (i.e. 43 cm). Presumably, the longer such a distance, the larger the window of opportunity for participants to readjust their response (e.g., withdraw a response on a NoGo trial before their hand reaches the response key). Future research with this or similar paradigms should involve a shorter distance between home and response keys, and thus, less opportunity for online adjustments in movement planning/execution.

Another disappointment of the current study was the absence of any significant associations between COMT and task performance. This absence may derive from our failure to discretely manipulate and measure the transitioning or switching of behaviour. As emphasized by Bilder et al. (2004), many of the cognitive paradigms used to examine COMT effects, are often complex in design, requiring both switching/transitioning to alternate network states (i.e., cognitive flexibility; reliant on val) and the maintenance of behavioural programming (i.e., cognitive stability; reliant on met). Although PREP and CON changed across trials, the requirements of the participant did not – i.e., participants must always Go when presented with a large physical gap and withhold a response (i.e., NoGo) when presented with a small gap. As such, successful performance on the AIT-R requires maintenance of behavioural programming across all conditions yet no actual task switching, even on conditions we hypothesized to be more or less reliant on met or val. Future research aimed at elucidating the relationship between COMT and cognitive functioning should aim to use tasks which orthogonally manipulate and measure the switching/transitioning and the maintenance of behavioural programs. A task requiring the rapid switching of rules (e.g., a task switching paradigm), for example, may more accurately reflect phasic DA activity (i.e., met-mediation).

General Discussion

The main framework of this thesis was to seek behavioural indicators consistent with the hypothesis that schizotypy is related to a disproportionate impairment on behavioural indices of dorsal trend functioning but relatively preserved functioning on those indicative of ventral trend functioning within tasks of AI. Ventral trend functioning among participants was inferred from their behavioural responses (error rate, response times) to increasing PREP demands. Dorsal trend functioning was gleaned from behavioural responses to increasing CON demands. It was hypothesized that schizotypy would be associated with manipulations of CON but generally unassociated with manipulations of PREP. Our hypothesis was based on theoretical claims (i.e., DDT [Christensen & Bilder, 2000], DOH [Giaccio, 2006]) as well as mounting empirical findings suggesting disproportionate dorsal trend impairment characterizes SCZ (Abruzzesse et al., 1995; Butler et al., 2001; Cavallaro et al., 2003; King et al., 2008). Comparison of findings across studies

Response conflict and action inhibition

Behavioural findings observed across the AI tasks used in Study 1 and Study 2 are largely consistent with one another. Most notably, increasing CON generally resulted in differential speeds of responding between Ave-SPQs and High-SPQs. In Study 1, conditions of hiCON (but not loCON) resulted in slower SURTs only among Ave-SPQs. In study 2, Ave-SPQs were found to have slower GoRTs across trials of hiCON but not loCON, relative to High-SPQs. The differential impact of CON demands was observed at early stages of movement, specifically as demonstrated by participants' HKRT. Within non-modulatory and SU trials in Study 1, Ave-SPQs had slower HKRTs on trials of hiCON, but not loCON. Ave-

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SPQs' HKRTs on Go trials of hiCON, but not loCON, in Study 2, were also slower, relative to High-SPQs.

Collectively, the differential impact of increasing CON demands between groups has been interpreted as reflecting impairment among High-SPQs in their ability to detect and/or decipher CON signals and modify their behaviour accordingly. These findings are consistent with those of previous studies showing that individuals with SCZ fail to invoke post-conflict adjustments in behaviour (Carter et al., 2001; Kerns et al., 2005). For example, using the Stroop, Kerns et al. (2005) found that persons with SCZ, relative to HCs, failed to demonstrate adjustments in performance on post-conflict and post-error trials. These findings have also been interpreted as reflecting impairment among persons with SCZ to detect CON. Similarly, Carter et al. (2001) found that SCZ patients fail to significantly reduce their RTs after errors of omission on a degraded version of the AX-CPT task. Notably, the AI task used by Carter et al. (2001) is similar to the AIT and AIT-R in that CON demands are intentionally taxed by degrading the decipherability of task stimuli. Our findings extend the investigations of Kerns et al. (2005) and Carter et al. (2001) by demonstrating impaired CON within the context of intact PREP functioning.

Botvinick and colleagues (2001, 2007) hypothesize that the ACC functions as an error detector which triggers compensatory behavioural adjustments. One such strategy – reducing ones' speed in the face of CON – has been observed across a wide range of task settings, including the flanker task (Gratton, Coles, & Donchin, 1992), the Stroop (Kerns et al., 2004), the Simon task (Sturmer, Leuthold, Soetens, Schroeter, & Sommer, 2002), and is interpreted as a reactive compensatory behaviour (Botvinick, 2007). In the current thesis, we interpret Ave-SPQs reduction in speed in the face of increased CON as a compensatory strategy which

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increases the efficiency of information processing by decreasing the cognitive resources required to manage hiCON.

These results are in keeping with previous findings within our laboratory showing the failure of SCZ to invoke compensatory behaviour/strategy use. When administering a memory paradigm to individuals with SCZ, McAnanama, Christensen & Lau (2005) found that people with SCZ are unable to utilize verbatim memory over gist memory even within conditions that cue verbatim memory strategy use. These findings were interpreted as suggesting that SCZ have a fault in strategic regulation of memory (McAnanama et al., 2005). Elahipanah, Christensen, & Reingold (2008) have recently found that persons with SCZ show a deficit in their ability to modulate their attentional span (size of attention spotlight) as dynamically as HCs under varying experimental conditions. Additionally, Bryan & Christensen (2003) found that even when SCZ patients were able to learn semantic clustering strategies they were not able to apply them to appropriately modify their behaviour – i.e., aid the recall of verbally presented information (Bryan & Christensen, 2003).

Interpreting our current results within Botvinick's (2007) model suggests possible ACC impairment among individuals with schizotypy, and that such impairment may be responsible for their failure to invoke compensatory strategies. This interpretation converges with functional imaging studies in which the caudal ACC in individuals with SCZ showed reduced activity during errors of commission elicited during a degraded stimuli CPT task. Employing Nuechterlein's (1983b) degraded stimuli version of the CPT, Honey et al. (2005) found that individuals with SCZ showed decreased activation within the ACC on trials involving degraded task stimuli. Within the same task, persons with SCZ also failed to show a task-specific association between the ACC and medial superior frontal gyrus (i.e., DLPFC) which

was observed in HCs. Kerns et al. (2005) also found individuals with SCZ to have reduced conflict-related activity within with ACC, relative to HCs.

More broadly, High-SPQs' disproportionate difficulty detecting and/or interpreting increased CON builds upon growing evidence of dorsal trend impairment in SCZ. Individuals with SCZ, for example, show marked deficits in behavioural tasks highly dependent on magnocellular input to the dorsal visual stream, such as motion detection and backward masking (Cadenhead et al., 1998; Chen et al., 2003; Green et al., 2003; Li, 2002) as well as susceptibility to visual illusions during reach-to-grasp behaviour (King et al., 2008). Functional imaging investigations have also provided more direct evidence for dorsal stream impairment among individuals with SCZ (Braus et al., 2002; Butler et al., 2001; Butler et al., 2007). Using fMRI, for example, Braus et al. (2002) found dorsal impairment within a sensory information processing paradigm which required participants merely to attend to moving visual stimuli and auditory stimuli. Compared to control participants, SCZ patients demonstrated reduced activation in the right thalamus, right PFC (i.e., at level of frontal eyefields and BA 46), and bilateral parietal lobes restricted to the dorsal visual pathway. Convergent findings have also been observed when employing EEG to identify neural correlates of viewing stimuli designed to bias the visual system towards either magnocellular (dorsal) or parvocellular (ventral) stimuli (Butler et al., 2001; Butler et al., 2005).

Measuring the impact of response conflict on action inhibition

It should be noted that our means of analyzing the impact of CON on RTs within tasks of AI differs from the conventional procedures used by various other groups (e.g., Kerns et al., 2005; Leung, Skudlarski, Gatenby, Peterson, & Gore, 2000). These groups typically analyze RTs on trials directly following hiCON trials (i.e, post-CON and post-error) in order to gauge

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the degree to which participants modify the speed of their behavioural responses when confronted with CON. Notably, these researchers typically also employ paradigms conducive to event-related analysis such as the AX-CPT (e.g., Carter et al., 2001) and the switching Stroop (e.g., Kerns et al., 2005). Our method of analysis was chosen to more closely reflect the method through which we manipulated CON demands. The AIT and AIT-R employed blocked designs (i.e., CON demands were held constant across the block of trials). For this reason, it seemed more appropriate to analyze the effects of increasing CON demands by comparing performance between, rather than within, blocks.

However, we also felt it was important to examine post-CON RTs given that such analysis remains convention within the field. Accordingly, we examined Go RTs on trials directly following trials involving a modulatory signal (i.e., either a SU or INH signal) in Study 1[3]. Analysis revealed a similar pattern of findings across both methods of analysis, although the post-CON analysis failed to reach statistical significance.

Response prepotency and action inhibition

Another important finding was that High-SPQ and Ave-SPQ were not differentially impacted by increasing PREP demands. For example, within Study 1 Ave-SPQs and High-SPQs' SU and INH error rates, as well as SURTs and HKRTs, were not differentially impacted by increases in PREP difficulty. Within Study 2, increasing PREP demands also failed to elicit a differential effect on groups' error rates (Go, NoGo), GoRTs, and GoHKRTs. These findings were interpreted as reflecting a relative sparring of AI, *per se*. These findings complement previous work in our laboratory challenging the view that the pathophysiological process of SCZ, per se, determines AI impairment among this population. Using the SSP (Logan &

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[3] Within the AIT-R, all trials (with the exception of the first) can be conceptualized as post-CON trials; thus a post-CON RT analysis would not have substantially differed from the blocked analysis we conducted and reported. Consequently, additional analysis on the AIT-R was not performed.

Cowan, 1984), Christensen and colleagues (Christensen & Daskalakis, 2002; Christensen, Wilson, and Daskalakis, 2010 [submitted]) found that medicated SCZ patients, but not unmedicated SCZ patients or HCs, showed AI impairment. With the aim of experimentally disentangling the effects of medication on AI from other potentially confounding factors inherent across SCZ membership (e.g., illness chronicity, hospitalization), the authors next administered a single oral dose of either olanzapine (an atypical antipsychotic), haloperidol (a typical antipsychotic), or placebo to HCs. Notably, only individuals on olanzapine, but not haloperidol or placebo, showed impaired AI on the SSP. These findings suggest that AI per se is relatively intact among persons with SCZ. Moreover, it demonstrates that olanzapine (and arguably other atypical antipsychotics) may be an important mechanism underlying the medication-related AI deficit that is associated with SCZ.

The current findings lead to the implication that persons with SCZ may show relatively preserved functioning among other functions sub-served by the ventral trend, including the OFC. Reversal learning and extinction, for example, have long been linked to OFC functioning (for review, see Happaney, Zelazo, & Stuss, 2004). Within tasks of reversal learning animals learn a simple discrimination between two objects (choice of one object is rewarded while the other is not). After this discrimination is learned to criterion, the rule is reversed (the previously unrewarded object is now rewarded). On these tasks, OFC-lesioned animals, as well as humans with acquired OFC damage, fail to switch their responses and perseverate on the initial discrimination (Boulougouris, Dalley & Robbins, 2007; Butter, 1969; Iversen & Mishkin, 1970; Rolls, Hornak, Wade, & McGrath, 1994). In response extinction tasks a response is initially reinforced, and then withheld. OFC-ablated non-human primates (e.g., Butter, Mishkin, & Rosvold, 1963) as well as human patients with OFC damage (Rolls et al., 1994) display

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resistance to extinction, continuing to respond to the non-reinforced stimulus. More broadly, acquired OFC damage among humans has been found to be associated with dysfunction on tasks in which an alteration of behavioural strategy is required in response to a change in environmental reinforcement contingencies (Goodglass & Kaplan, 1979; Jouandet & Gazzaniga, 1979; Kolb & Whishaw, 1996).

These findings, among others, have lead Rolls (2004) to develop a formalized theory of OFC functioning which centres on its role in stimulus-reinforcement association learning. Rolls (2004) further hypothesizes that dysfunction in stimulus-reinforcer learning may underlie the behavioural changes observed clinically with individuals with OFC damage. Supporting this claim are findings of associations between the degree of OFC damage and observations of disinhibited or socially inappropriate behaviour, misinterpretation of other people's moods, impulsiveness, unconcern of underestimation of the seriousness of their condition, and lack of initiative (Rolls et al., 1994). Rolls has proposed that insensitivity to shifts in reward contingencies may, at least to some extent, contribute to the observed changes in behaviour among humans with OFC damage. Of note, this theoretical framework allows for deficits on the IGT and OAT, tasks well accepted as relying on OFC-mediation, to be understood as consequences of a single mechanism (i.e., an insensitivity to reward contingencies). Developmental studies have identified preschool age (i.e., 3-4 years of age) as a critical stage during which sensitivity to OFC-mediated functions are largely acquired. Using a simplified version of the IGT (i.e., the Children's Gambling Task; [CGT]), for example, Kerr & Zelazo (2004) showed that sensitivity to reward contingencies is acquired during this developmental stage. Using a test of object reversal learning, Overman, Bachevalier, Schulhmann, and Ryan

(1996) have found a similar developmental time frame within which humans initially acquire sensitivity to reward contingencies.

Among individuals with SCZ, there is indeed growing evidence to suggest a relative sparing of ventrally-mediated functioning (Abruzzese et al., 1995; Bechara et al., 1994). Particularly compelling, in reference to the theoretical claims of Rolls (2004), are observations of intact functioning across the IGT, (Bechara et al., 1994; Cavallaro et al., 2003; Wilder et al., 1998) and the OAT (Abruzzese et al., 1995; Abruzzese et al., 1997). These findings suggest that persons with SCZ may also show preserved functioning on other tasks requiring sensitivity to reward contingencies.

These findings converge with various other investigations conducted with individuals with SCZ that suggest intact functioning on ventrally mediated tasks. For example, intact performance on tasks requiring bias toward visual details over context (Place & Gilmore, 1980), the use of non-motion cues to process motion (Chen et al., 1999), the ability to process automatic and prepotent elements of basic visual information (Chey & Holzman, 1997), identification of target letters in a backward masking paradigm (Cadenhead et al., 1998), visual size estimation under illusion conditions (King et al., 2008), normal ERP activation in conditions that bias processing towards the parvocellular (ventral) pathway (Braus et al., 2002), emotional modulation of the startle reflex (Curtis, Lebow, Lake, Katsanis, & Iacono, 1999; Schlenker, Cohen, & Hopmann, 1995), and attentional orienting (for review, see Gold, Hahn, Strauss, et al., 2009).

Discrepant findings across studies

A notable discrepancy was observed between results from AIT and AIT-R. In Study 1 Ave-SPQs slowed their HKRT on INH trials as CON increased. Similar to the other

performance indices discussed above (e.g., SURT, GoRT, HKRT on Go trials), this finding was interpreted as reflecting impairment among High-SPQs in their ability to detect and/or decipher CON. Unexpectedly, however, groups' NoGoHKRTs observed in Study 2 were not disproportionately impacted by increasing CON demands. Although these findings initially appear inconsistent with those of Study 1, this discrepancy may reflect differences in task demands (e.g., AIT is a SSP while AIT-R is a Go/NoGo paradigm).

To review, in AIT-R participants' NoGoHKRTs were shorter on trials of loCON, relative to hiCON. These findings may reflect the fact that the participant is signaled before the initiation of movement (e.g., when a Go/NoGo design is implemented as opposed to a SSP). In this scenario participants are not required to make online adjustments or recalibrations in response to modulatory stimuli (e.g., the stimuli signaling them to INH or SU their already-initiated movement). Discrepant INH HKRTs between groups on the AIT may reflect a particular weakness among High-SPQs in the detection and/or processing of conflict when required to do so at a later stage of movement. To be clear, however, our findings support a deficit in detecting and/or deciphering CON at earlier stages of movement among High-SPQs as well (e.g., absence of behavioural adjustments in, SU HKRTs, INH HKRTs in AIT, GoHKRTs in AIT-R). Collectively, our findings instead suggest that High-SPQs find hiCON particularly taxing when "online" processing and sustained monitoring is required.

Schachar et al. (2007) have recently theorized that discrepancies in performance across Go/NoGos and SSPs, such as those observed in the current study, may reflect reliance on differential inhibitory control mechanisms. Although the literature largely assumes similar inhibitory controls across Go/NoGo and SSP tasks (e.g., Aron et al., 2004), Schachar et al. (2007) argue that Go/NoGo tasks require *action restraint*, the ability to withhold a strong

response tendency of a preplanned action. In comparison, SSPs require participants to cancel an ongoing preplanned action, which they define as *action cancellation*. Using Schachar et al.'s (2007) nomenclature, AIT requires action cancellation while AIT-R requires action restraint (Schachar et al., 2007).

In a recent review, Eagle et al. (2008) present evidence suggesting that these forms of AI may also be dissociable at a neuroanatomical and neuropharmacological level. Imaging studies typically implicate bilateral involvement (e.g., right and left IFG) in action restraint whereas the right hemisphere alone (e.g., right IFG) mediates action cancellation (Aron et al., 2003; Bunge et al., 2002; Garavan et al., 1999; Konishi et al., 1999; Koshi et al., 1998; Menon et al., 2001).

Research findings pointing to discrepant neuropharmacological pathways between action restraint and action cancellation provide particularly compelling evidence for their neurobiological divergence. Numerous findings across rodent and human studies support the role of serotonin (5-HT) in action restraint (Harrison, Everitt, & Robbins, 1999; Vollm, Richardson, McKie, Elliott, Deakin, & Anderson, 2006). In contrast, 5-HT has only rarely been implicated in action cancellation (Crean, Richards, and de Wit, 2002). Additionally, studies using rats and humans implicate noradrenaline as a candidate neurotransmitter in the mediation of action-cancellation. The selective noradrenaline reuptake inhibitor, atomoxetine, for example, was found to decrease SSRTs in humans and rats (Chamberlain, Muller, Blackwell, Clark Robbins, & Sahakian, 2006; Robinson, Eagle, Mar, Bari, Banerjee, Jiang, Dalley, & Robbins, 2008). Relatively fewer studies directly address the role of noradrenaline in action restraint making the determination of any differential impact of noradrenaline upon these separate forms of AI difficult (for review, see Eagle et al., 2008).

The pattern of behavioural findings observed in AIT and AIT-R suggests that inhibitory HKRTs among High-SPQs are differentially impacted by increases in CON (relative to Ave-SPQs) only within tasks requiring action cancellation, but not action restraint. Caution, however, should be taken when extrapolating from findings reported by Schacher et al. (2007) and Eagle et al. (2008) to understand functioning in SCZ, as they focus on mechanisms of inhibitory control within tasks of action inhibition. Notably, our findings suggest that High-SPQs may show impairment on tasks of AI because of difficulty in detecting and/or interpreting environmental cues of hiCON in general, not just those signaling inhibition.

Kinematic data

Inclusion of kinematic analyses in Study 1 represents the first investigation (known to the author) to examine the kinematics of High-SPQs within a task of AI. In doing so, the findings of Study 1 help clarify the unique contributions of PREP and CON demands at various stages of the planning/execution of movement within AI. Overall, participants were found to reach a higher velocity on trials in which the modulatory signal was presented relatively later (i.e., conditions of hiPREP). These results suggest that the presentation of a SU signal interferes with, rather than facilitates, participants' ability to speed-up their response.

Participants were also observed to have marginally higher peak velocities on trials of loCON, as opposed to hiCON, presumably because of the lower cognitive resources required in interpreting/deciphering task stimuli of loCON. With regard to group differences, High-SPQs reached marginally higher peak velocities, relative to Ave-SPQs, when receiving SU signals later, rather than earlier. This finding may suggest that even when presented later, the SU signal causes less interference with motor planning/execution among High-SPQs than it does to Ave-SPQs. That High-SPQs are less influenced, relative to Ave-SPQs, by the presentation

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of modulatory signals was interpreted as reflecting their general deficit (as inferred from SURTs and HKRTs) in detecting and/or interpreting the meaning of SU and INH stimuli.

Overall, participants were found to reach their peak velocities earliest when the following conditions were both met: loCON and hiPREP. That is, in the least taxing condition (when stimuli were relatively easy to discriminate and the modulatory signal appeared relatively farther into ones' movement planning and/or execution), participants reached their peak velocities sooner. Of note, Ave-SPQs and High-SPQs were found to need a similar amount of time to reach their peak velocities across all task conditions. Thus, High-SPQs' faster HKRTs and SURTs on conditions of hiCON can not be accounted for by an ability to more quickly reach peak velocity. By extension, they support the argument that the differential impact of CON is initially experienced at a relatively earlier stage of movement planning/execution (e.g., HKRTs).

This finding is particularly important when considering the dichotomy between the planning of a visuomotor action and its on-line control, a topic reviewed by Glover (2004). Glover's (2004) model outlines a planning system which is responsible for selecting and initiating an adaptive motor program given the environment and the goals of the actor, as well as the control system which provides monitoring and the occasional adjustment of motor programs in flight. Within the context of the current study, the planning system would be responsible for selecting and initiating a motor program consistent with the task demands (i.e., speeding up a response when presented with a large gap and inhibiting a response when presented with a relatively smaller gap). The planning system also determines the initial kinematic parameterization of the movements, including their timing (e.g., HKRT) and velocity.

The control system, in contrast, provides monitoring and the occasional adjustment of motor programs in flight. These adjustments are limited to spatial characteristics of the target. The control system may intervene, for instance, if spatial errors arose for some reason (e.g., interference from cognitive influences, noise in the neuromuscular system, unexpected shift in target location). These two stages of movement are temporarily overlapping, in order to provide smooth rather than jerky movement correction. Thus, while the planning system is highly influential prior to movement initiation, and in fact, continues to be very influential early in the movement, the influence of the control system on the spatial parameters of the action increases throughout the course of ones' movement.

Collectively, the pattern of results observed across Study 1 (e.g., SU-HKRTs, SURTs, PVs, TTPVs) argue that the planning system conceived by Glover (2004) is largely responsible for detecting and/or deciphering CON and PREP demands within action cancellation. Furthermore, High-SPQs were differentially impacted by increased CON demands, but not PREP demands, relative to Ave-SPQs. Taken together these findings suggest that High-SPQs show a disproportionate impairment on dorsally-mediated deficits within the planning system. In this way, our findings are consistent with those of Carnahan and colleagues (Carnahan, Elliott, & Velamoor, 1995; Carnahan, Aguilar, Malla, & Norman, 1997) which reveal that motor abnormalities among persons with SCZ may reflect greater deficits in motor planning than problems with movement execution. For example, Carnahan, Aguilar, Malla, & Norman (1997) conducted an experiment in which patients with SCZ and controls performed aiming movements using a mouse towards targets of different sizes and distances appearing on a computer screen. Movement planning was assessed by establishing the reaction time to initiate movement following a cue. Movement execution was determined by measuring movement

time from the onset of movement to its termination. In healthy individuals, movement planning and execution has been shown to follow a number of regularities that are known as Fitts' Law. According to Fitts (as cited in Carnahan et al., 1997) the time of a person's aiming movement is logarithmically related to the amplitude of the movement and the width or size of the target. Thus faster (or shorter) aiming movements are made to closer and larger targets while aiming movements are slower (or longer) to farther and smaller targets. In this context, deficits in movement execution are suggested by aiming movements that do not conform to these expected patterns.

Both leucotomized and non-leucotomized SCZ patients demonstrated longer reaction times and a left hand advantage for movement preparation that was not seen in controls. However, no differences in movement time were noted between groups. That is, both groups' performance conformed to the expected patterns as specified by Fitts' Law. Movement times were comparable in both groups and faster to the large and near targets and slower to the small and farther targets. These results provide evidence that motor slowing in individuals with SCZ may reflect deficits in movement planning rather than problems with movement execution.

Notably, conclusions regarding the kinematics of AI among SCZ may be limited to understanding behaviour within tasks of action cancellation. As shown when comparing HKRTs on inhibitory trials between AIT and AIT-R High-SPQs show particular impairment in detecting and/or processing hiCON when the task demands involve action cancellation, as opposed to action restraint. Thus, conclusions drawn regarding the involvement of the planning system in AIT (a task of action cancellation) may not necessarily generalize to the tasks of action restraint.

COMT

Unexpectedly, COMT genotype was not found to significantly relate to group membership (i.e., Ave-SPQ, High-SPQ). Notably, however, such findings are not uncommon among studies examining the role of COMT in the development of SCZ-spectrum disorders. For example, although preferential transmission of the high activity val allele to SCZ offspring has been observed by some (Egan et al., 2001; Li et al., 1996; Kunugi et al, 1997; Li et al., 2000), others have failed to find a similar association (Karayiorgou et al., 1998; Strous et al., 1997; Wei & Hemmings, 1999).

In Study 2, COMT genotype was also not found to significantly impact participants' performance on the AIT-R, including error rates, GoRTs, or HKRTs in response to increasing PREP and CON demands. These findings fail to reconcile the largely inconsistent existing literature examining the relationship between COMT genotype and cognition found among individuals with SCZ as well as HCs. For instance, the val allele has been found to be associated with poorer performance on prefrontally-mediated cognitive tasks among individuals with SCZ, such as executive functioning, processing speed, and attention (Egan et al., 2001; Weinberger et al., 2001; Bilder et al., 2002; Goldberg et al., 2003; Han et al., 2006). Among HCs, the met allele has been found to be associated with significantly fewer perseverative errors on the WCST (Malhotra, et al., 2002) while individuals with the met/met genotype perform better on Trail Making Test-B (Sheldrich et al., 2008), tests of executive functioning, and visuospatial tasks (Bruder et al., 2005; de Frias, et al., 2005). Others studies, in contrast, have failed to show a relationship between COMT and cognitive functioning (Stefanis et al., Van Os, 2004; Tsai et al., 2003; for review, see Glatt et al., 2003).

The current dissertation sought to test Bilder et al.'s (2004) proposal that the variability of findings observed within these studies may be due, in part, to the differential effect of the COMT Val[158]Met alleles on different types of cognitive tasks. As emphasized by Bilder et al. (2004), many of the cognitive paradigms used to examine COMT effects, are often complex in design, requiring both switching/transitioning to alternate network states (i.e., cognitive flexibility; reliant on val) and the maintenance of behavioural programming (i.e., cognitive stability; reliant on met). In reviewing studies examining COMT effects on cognition, Bilder et al. (2004) highlighted findings from Nolan et al. (2004) which demonstrated that switch costs (a measure of met functioning), shared a large percentage of variance with COMT genotype. Of relevance, Nolan et al.'s (2004) paradigm was much more straight-forward and less complex than the AIT-R. Thus, our null findings may reflect our failure to discretely manipulate and measure met- and val-mediated functions within the AIT-R. For example, unlike Nolan et al.'s (2004) paradigm, the AIT-R does not have a true task switching component. Although the decipherability of task stimuli changes across trials, the requirements of the participant does not change or switch throughout the task – i.e., participants must always Go when presented with a large gap and always withhold a response (i.e., NoGo) when presented with a small gap. As such, successful performance on the AIT-R requires maintenance of behavioural programming across all conditions yet no actual task switching, even on conditions we hypothesized to be more or less reliant on met or val. To summarize, the absences of a significant effect of COMT genotype on AIT-R performance may reflect a lack of discrete operationalization of met- and val- mediated functioning within our task.

COMT genotype was, in contrast, found to correlate with certain clinical measures administered during Study 2. Met homozygotes had significantly higher scores on the Positive

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Impression Management subscale of the PAI relative to both val/vals and met/vals. Met homozygotes also had significantly lower scores on the Gregariousness facet of the Extraversion domain on the NEO-PI than met/vals but not val/vals. Met/vals and val/vals did not significantly differ on this measure. These findings were in keeping with previous studies showing met homozygotes to have lower Extraversion Factor scores on the NEO-FFI (Hoth et al., 2006; Reuter & Henning, 2005). Of note, Extraversion, a factor shown to be heritable (Jang, Livesley, Vernon, & Vernon, 1996) has been found to be negatively associated with several anxiety disorders (e.g., agoraphobia and social phobia; Bienvenu & Stein, 2003; Bienvenu et al., 2001). Thus, it is possible that the met homozygotes have a predilection to express low Extraversion (i.e., introversion), as captured on the NEO-PI, and that such expressions of introversion increase one's susceptibility of (or at the very least as associated with) developing an anxiety disorder.

Study limitations and future directions

The current thesis did not yield differential error rates (across either INH/NoGo or SU/Go trials) between Ave-SPQs and High-SPQs. One might expect that the slower SURTs (AIT) and GoRTs (AIT-R) in conditions of hiCON observed among Ave-SPQs would confer advantage by increasing ones' chances of correctly inhibiting a prepotent response on an INH trial. However, this pattern of results was not observed. Importantly, our task differs from many AI tasks in that the response key is relatively far away from the home key (i.e., 43 cm). Due to this design, participants were afforded a larger window of opportunity within which to potentially "correct" their response on an INH trial. In other words, if a participant initiates movement on an INH trial by releasing his/her hand from the home key and accelerating towards the response key, it is possible that part way into this movement sequence the

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participant may recognize the response error and retract the hand before depressing the response key. Among AI tasks in which participant's fingers rest upon the response key such course corrections seem relatively unlikely. It is recommended that future studies employing the AIT or AIT-R modify apparatus by decreasing the distance between the home key and response key (e.g., decrease to 10 cm).

The current thesis also did not show significant relations between COMT and either schizotypy or cognition. Future research aimed at elucidating the relation between COMT and cognitive functioning should aim to use tasks which orthogonally manipulate and measure the switching/transitioning and the maintenance of behavioural programs. A task requiring the rapid switching of rules (e.g., a task switching paradigm), for example, may more accurately reflect phasic DA activity (i.e., met-mediation). More broadly the inconsistent findings in this area suggest a need for a better understanding of the behavioural domains governed by COMT.

A limitation of the current study is the questionable degree to which our results, obtained with relatively high-functioning undergraduate university students, are generalizable to individuals with more florid symptoms of SCZ (e.g., those meeting DSM-IV [American Psychiatric Association, 1994] criteria for schizophrenia). Our sample of High-SPQs, for example, was found to have similar estimated IQs to our control sample, an uncommon finding among studies using individuals with SCZ-spectrum disorders. In order to address this concern, future studies should administer the AIT-R task to individuals with diagnosed Schizophrenia. Given the potential contribution of atypical antipsychotics on AI (Christensen et al., submitted) it would also be advised that such an investigation involve neuroleptic naïve or unmedicated individuals with SCZ.

An obvious limitation of the study centres on the fact that conclusions drawn regarding brain functioning are only inferential. In substantiating our theoretical claims regarding the integrity of the dorsal mediation of CON and the ventral mediation of PREP, and its relevance to understanding functioning in SCZ, future studies will require functional imaging technologies such as fMRI and ERP. Previous investigations examining the neural underpinnings of PREP and CON among HCs implicate the IFG in the mediation of PREP and the ACC in the mediation of CON across various tasks. Indeed, a functional and structural dissociation of PREP and CON was found in a recent fMRI study by Matthews et al. (2005), in which these constructs are measured independently within the same Go/NoGo task. Matthews et al. (2005) found increased activation in the right IFG in hiPREP, relative to loPREP conditions. CON-related activity was assessed by comparing neural activation between correct and incorrect NoGo trials. Increased neural activation was observed in the right/left dorsal ACC during incorrect, compared to correct, trials. These findings suggest, firstly, that PREP and CON demands are dissociable at an anatomical level, and, secondly, that such dissociation is observable within the same paradigm. This knowledge has not yet been brought to bear on our understanding of SCZ.

No previous study has independently manipulated RI and CON within the same task among SCZ while concurrently investigating associated neurophysiological activation. To test this theory, future research could include the use of the AIT-R in conjunction with fMRI technology. An event-related fMRI design could allow for the examination of 1) the ACC's role in detecting CON, 2) the role of the IFG in detecting PREP, 3) the role of the ACC in recruiting the DLPFC during AI, 4) the role of the ACC (by way of the DLPFC) in predicting behavioural adaptations during AI, and finally understanding 5) how activation among persons

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with SCZ differ in relation to HCs, with a particular interest in how the ACC mediates any diverging activation and behaviour. In considering relevant empirical findings (e.g., Carter et al. [2001], Kerns et al. [2005] and the current findings) as well as theories of ACC functioning, I would hypothesize that AI deficits among persons with SCZ would be found to be mediated by impairment within the ACC.

The neural circuitry underlying the relative contributions of CON and PREP in producing AI deficits in SCZ could also be investigated using ERP technology. Of relevance, the literature suggests that NoGo P3 amplitude is a neurophysiological marker of ACC activation, DLPFC recruitment, and behavioural adaptation in the face of CON, while N2 amplitude is an index of PREP (for review, Zordan et al., 2008). N2 component amplitude, for example, is recorded between 250 and 450 ms over central locations in NoGo vs. Go trials and is thought to constitute a marker of AI (Dockree et al., 2005; Falkenstein et al., 1995). In contrast, the P3 component, observed on both Go and NoGo trials has been viewed as a marker of stimuli evaluation and/or CON resolution, functions consistent with our conceptualizations of CON (Falgater & Strik, 1999; Zordan et al, 2008; Pfefferbaum & Ford, 1988; Ford et al., 2004). Thus, ERP could be a useful tool for distinguishing the relative role of different neural systems, associated with CON and RI, respectively, in producing AI impairment in persons with SCZ. Specific aims of such a study should include (1) testing for convergent ERP evidence to corroborate the current behavioural findings of a relative deficit in CON processing (as indexed by NoGo P3 amplitude) as compared to AI *per se* (as indexed by N2 amplitude), in individuals with SCZ. It should also test for evidence that CON processing deficits contribute to AI impairment in SCZ, by examining whether a neurophysiological marker of CON processing deficits (reduced NoGo P3 amplitude) correlates, across patients, with increased PREP demands.

Clinical implications

That AI impairment in SCZ may be an artifact of CON demands has important clinical implications. First, it brings into question our current understanding of the neuropsychological profile of SCZ, of which action inhibition, as measured by instruments such as the WCST, Go/NoGo, and SSP, is typically considered impaired (Laws, 1999). By extension, these findings highlight the need for neuropsychological measures of higher specificity. For instance, in order to achieve a more accurate understanding of cognitive impairment within SCZ, the development of neuropsychological measures capable of independently measuring AI (and other ventrally-mediated cognitive functions such as reversal learning or probabilistic reasoning), free from the confounds of dorsally-mediated constructs such as CON, will be critical.

The current findings also lead to the expectation that individuals with SCZ-spectrum disorders will show impairment on various tasks in which relevant information/instruction is presented in ways that is difficult to decipher and interpret and/or difficult to distinguish from competing or irrelevant information. When planning and implementing treatment protocols for individuals with SCZ, for example, information should be presented in ways that are highly decipherable and interpretable to this population. Our findings suggest that information not clearly presented will be less likely to direct and guide behaviour as intended and appropriate.

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Appendix

Appendix A. Telephone recruitment script for study 1

TELEPHONE RECRUITMENT MESSAGE

Experimenter: *"Hi, may I please speak with [STUDENT NAME]."*
Potential Participants: *"This is STUDENT NAME, how may I help you?"*

Experimenter: *"My name is Carolyn Wilson. I am a graduate student in the Department of Psychology at the University of Waterloo. I work under the supervision of Dr. Bruce Christensen, and I am calling to inquire whether you are interested in participating in a study we are conducting on personality dimensions and motor skill. The experiment will take about 2 hours of your time, and you will receive 2 participation credits. If you think you might be interested, I can provide you with some more information."*

If NOT interested: Thank student for their time and discontinue conversation.

If interested: *"The experiment involves completing some tasks on the computer that have been designed to examine your speed and accuracy in responding to cognitive stimuli. Specifically, we are interested in how certain personality features, such as creativity, relate to your performance on these tasks. We will also have you complete a card sorting task as well as watch a videotape of another individual sorting cards during which we will ask you to evaluate their performance".*

"This study has been reviewed and received ethics clearance through the Office of Research Ethics, and therefore, you are free to withdraw from it at any point in time without penalty or loss of participation credits. The final decision about participation is yours. All information you will provide is strictly confidential, and no identifying information will appear on any of the study materials.

"Would you like to participate?"

If interested say: *"I have several openings within the next couple of weeks, are there any times that are particularly convenient for you?"*

"Thanks – I'll see you on [APPOINTMENT TIME]. In the meantime, if you have any questions or concerns, please feel free to contact me by e-mail (cmwilson@watarts.uwaterloo.ca)"

Appendix B. E-Mail recruitment script for study 1

E-MAIL RECRUITMENT MESSAGE

Dear [student name]:

I am writing to inquire whether you are interested in participating in a study we are conducting on personality dimensions and motor skills. The experiment will take about 2-hours of your time, and you will receive 2 participation credits.

The experiment involves completing some tasks on the computer that have been designed to examine your speed and accuracy in responding to cognitive stimuli. Specifically, we are interested in how certain personality features, such as creativity, relate to your performance on these tasks. We will also have you complete a card sorting task as well as watch a videotape of another individual sorting cards during which we will ask you to evaluate their performance.

This study has been reviewed and received ethics clearance through the Office of Research Ethics and that you are free to withdraw from it at any time without penalty or loss of participation credits. The final decision about participation is yours. All information you provide is strictly confidential, and no identifying information will appear on any of the study materials. If you are interested in participating please indicate so by replying to this e-mail. I will then suggest a series of possible appointment times for you to attend, and directions to the building and room.

Thank you for your consideration of this request.

Sincerely,

Carolyn Wilson
Graduate Student.

Appendix C. Cover Sheet, Consent Forms, and Debriefing and Education Feedback Forms

Title of Project:	Personality and Motor Skills
Principal Investigator:	Dr. Bruce Christensen
	Department of Psychology
	University of Waterloo
	Office Telephone: (416) 535-8501, ext. 6843
	Email: Bruce_Christensen@camh.net
Student Investigator:	Carolyn Wilson
	Department of Psychology
	University of Waterloo
	Email:cmwilson@watarts.uwaterloo.ca

Directions

Attached to this introduction is a detailed Consent Form that outlines the purpose of the experiment and your rights as a research participant. If you are still interested in participating in this project after reading the materials, please sign both copies of the consent form and keep one for your own records. The experiment will proceed in the following manner.

1. You will first be asked to complete a series of computer tasks that test speed and accuracy of motor responses to cognitive stimuli.

2. Next, you will first be required to complete a questionnaire that asks you for various demographic details about yourself such as age, native language, and medical history.

3. Next, you will complete a series of questionnaires enquiring about your current feelings, thoughts, and behaviour.

4. Next, you will complete a few problem-solving tasks.

> ❖ **In order to ensure confidentiality, please <u>DO NOT</u> record your name anywhere on the questionnaire.**
>
> ❖ **Please read each question carefully and make a quick decision as to which response best describes you.**

5. At the end of the study, you will be fully debriefed and provided with an educational feedback form. Additionally, you will be given the opportunity to ask the research assistant or graduate student any questions that you might have.

    Thank you in advance for your assistance with this project.

If you have any questions about the experiment, please ask the experimenter now before proceeding any further with the study.

Information Letter and Consent Form (for Credit)

Title of Project: Personality and Motor Skills

Principal Investigator: Dr. Bruce Christensen
                                            Department of Psychology
                                            University of Waterloo
                                            Office Telephone: (416) 535-8501, ext. 6843
                                            Email: Bruce_Christensen@camh.net

Student Investigators: Carolyn Wilson
                                            Department of Psychology
                                            University of Waterloo
                                            Email:cmwilson@watarts.uwaterloo.ca

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You are invited to participate in an experiment that involves completing some tasks on the computer that have been designed to examine your speed and accuracy in responding to cognitive stimuli. You will also complete a questionnaire that asks for various demographic details about yourself such age, native language, and medical history. In addition, you will also complete a series of paper and pencil questionnaires that ask you about your thoughts, feelings, and behaviour. Specifically, we are interested in how certain personality features, such as creativity, relate to your performance on these tasks. Participation in this study is voluntary. The study will take approximately 2.5-hours and you will receive 2 participation credits for your time.

By volunteering in the present project, you will learn more about psychological research in general, and the topics of this study in particular (i.e., personality features and motor skills). At the end of the study you will be provided with a detailed feedback sheet outlining the research project. There are no physical risks to participating in the study. However, you may experience some degree of frustration while carrying the computer tasks.

You are free to withdraw from the study at any point without penalty or loss of participation credits. If you would like to discontinue, simply inform the individual conducting the experiment (i.e., research assistant or graduate student). You may decline to carry out any of the tasks involved in the study. All the information you provide will be kept strictly confidential. Your name and/or student ID number will not be associated with any of the research materials. Consent forms will be stored separately from the questionnaire and experimental data so your identity cannot be matched with your responses in the experiment. In accordance with the Canadian Psychological Association research guidelines, the raw data will be stored in a locked room for seven years after completion of the study, at which point it will be destroyed. Only individuals authorized by Dr. Christensen will have access to the data during this period.

This study has been reviewed by and has received ethics clearance from the UW Office of Research Ethics. If you have any concerns about your participation in this study, you may

contact Dr. Susan Sykes, Director of the Office of Research Ethics (888-4567, ext. 6005). If you have questions or concerns about the study itself or your reaction to it, you may discuss them with the student investigator, Carolyn Wilson (cmwilson@watarts.uwaterloo.ca) or with Dr. Bruce Christensen ((416) 535-8501, ext. 6843; Bruce_Christensen@camh.net). Dr. Christensen is a licensed psychologist who specializes in the assessment and research of cognitive functioning. You may also contact UW Counseling Services at 888-4567, ext. 2655 if you feel you may need ongoing assistance with any personal difficulties.

Thank you for your assistance in this project.

I agree to participate in a study conducted by Bruce Christensen and Carolyn Wilson on personality and motor skills. I have made this decision based on the information I have read in the Introductory Sheet and Consent Form and have had all my questions about participating in the experiment addressed by the experimenter. I understand that I may withdraw this consent at any time by declaring this intention to the experimenter. I realize that I will not incur any penalty or lose my participation credits for withdrawing my consent. I also understand that this project has been evaluated by and received ethics clearance from the UW Office of Research Ethics. If I have any concerns about this study I can contact Dr. Susan Sykes, Director of the UW Office of Research Ethics at 888-4567, ext. 6005

If you are willing to participate in this experiment, please sign both copies of the Consent Form and keep one copy for your records.

Participant's Name (please print):   _____

Participant's Signature: _____

Date: _____

Witness' Name (please print):   _____

Witness' Signature: _____

Date: _____

Information Letter and Consent Form (for Pay)

Title of Project: Personality and Motor Skills

Principal Investigator: Dr. Bruce Christensen
Department of Psychology
University of Waterloo
Office Telephone: (416) 535-8501, ext. 6843
Email: Bruce_Christensen@camh.net

Student Investigator: Carolyn Wilson
Department of Psychology
University of Waterloo
Email:cmwilson@watarts.uwaterloo.ca

You are invited to participate in an experiment that involves completing some tasks on the computer that have been designed to examine your speed and accuracy in responding to cognitive stimuli. You will also complete a questionnaire that asks for various demographic details about yourself such age, native language, and medical history. In addition, you will also complete a series of paper and pencil questionnaires that ask you about your thoughts, feelings, and behaviour. Specifically, we are interested in how certain personality features, such as creativity, relate to your performance on these tasks. Participation in this study is voluntary. The study will take approximately 2.5-hours and you will receive \$8 per hour for your time.

By volunteering in the present project, you will learn more about psychological research in general, and the topics of this study in particular (i.e., personality features and motor skills). At the end of the study you will be provided with a detailed feedback sheet outlining the research project. There are no physical risks to participating in the study. However, you may experience some degree of frustration while carrying the computer tasks.

You are free to withdraw from the study at any point without penalty or loss of participation credits. If you would like to discontinue, simply inform the individual conducting the experiment (i.e., research assistant or graduate student). You may decline to carry out any of the tasks involved in the study. All the information you provide will be kept strictly confidential. Your name and/or student ID number will not be associated with any of the research materials. Consent forms will be stored separately from the questionnaire and experimental data so your identity cannot be matched with your responses in the experiment. In accordance with the Canadian Psychological Association research guidelines, the raw data will be stored in a locked room for seven years after completion of the study, at which point it will be destroyed. Only individuals authorized by Dr. Christensen will have access to the data during this period.

This study has been reviewed by and has received ethics clearance from the UW Office of Research Ethics. If you have any concerns about your participation in this study, you may contact Dr. Susan Sykes, Director of the Office of Research Ethics (888-4567, ext. 6005). If you have questions or concerns about the study itself or your reaction to it, you may discuss them with the student investigator, Carolyn Wilson (cmwilson@watarts.uwaterloo.ca), or with Dr. Bruce Christensen ((416) 535-8501, ext. 6843; Bruce_Christensen@camh.net). Dr. Christensen is a licensed psychologist who specializes in the assessment and research of cognitive functioning. You may also contact UW Counseling Services at 888-4567, ext. 2655 if you feel you may need ongoing assistance with any personal difficulties.

Thank you for your assistance in this project.

I agree to participate in a study conducted by Bruce Christensen and Carolyn Wilson on personality and motor skills. I have made this decision based on the information I have read in the Introductory Sheet and Consent Form and have had all my questions about participating in the experiment addressed by the experimenter. I understand that I may withdraw this consent at any time by declaring this intention to the experimenter. I realize that I will not incur any penalty or lose my participation credits for withdrawing my consent. I also understand that this project has been evaluated by and received ethics clearance from the UW Office of Research Ethics. If I have any concerns about this study I can contact Dr. Susan Sykes, Director of the UW Office of Research Ethics at 888-4567, ext. 6005

If you are willing to participate in this experiment, please sign both copies of the Consent Form and keep one copy for your records.

Participant's Name (please print):   _____

Participant's Signature: _____

Date: _____

Witness' Name (please print):   _____

Witness' Signature: _____

Date: _____

Debriefing and Education Feedback Form

Title of Project: Personality and Motor Skills

Principal Investigator: Dr. Bruce Christensen
                                  Department of Psychology
                                  University of Waterloo
                                  Office Telephone: (416) 535-8501, ext. 6843
                                  Email: Bruce_Christensen@camh.net

Student Investigators: Carolyn Wilson
                                  Department of Psychology
                                  University of Waterloo
                                  Email:cmwilson@watarts.uwaterloo.ca

In the present study we asked you to complete a number of computer tasks, as well as a series of questionnaires. The primary focus of the project was to refine novel tasks used to examine how certain personality features, such as openness to experience and creativity, relate to motor skills such as velocity and accuracy of movement.

We know that people who share these types of personality features can often be very sensitive to emotional stimuli. By looking at your motor responses to emotional stimuli, such as the pictures you viewed on the computer screen, we aimed to further develop this objective measure of your responses to such stimuli.

We also know that these personality features can influence how we organize information and solve problems. By examining your motor responses to the different stimuli that appeared on the computer screen, we aimed to investigate measures that could accurately depict the association between personality dimensions and your problem-solving abilities.

The questionnaire that you completed was used to enable us to further characterize your current feelings, thoughts, and experiences.

Thank you for your participation in the current study. Your efforts are greatly appreciated.

If you have any questions or concerns about this study, please feel free to contact Carolyn Wilson (cmwilson@watarts.uwaterloo.ca) or Dr. Bruce Christensen Bruce_Christensen@camh.net; 888-4567, ext. 3052). Dr. Christensen is a licensed Psychologist who specializes in understanding cognitive processes in various clinical populations.

If you feel at all concerned about the items on the questionnaire you completed during the experiment, please contact Dr. Christensen. You may also wish to contact UW Counseling Services (888-4567, ext. 2655). More generally, if you have any concerns about your

participation in this study you may contact Dr. Susan Sykes, who is the Director of the UW Office of Research Ethics (888-4567, ext. 6005).

References

Kleinsorge, T. (2001). The time course of effort mobilization and strategic adjustments of response criteria. *Psychological Research*, *65,* 216 – 223.

Rothermund, K., Wentura, D., & Bak, P.M. (2001). Automatic attention to stimuli signaling chances and dangers: moderating effects of positive and negative goal and action contexts. *Cognition and Emotion, 15 (2),* 231 – 248.

Personality and Motor Skills Study Payment Record Form

This hereby certifies that

_____

received $_____ for his/her involvement in the Personality and Motor Skills Study

conducted at The University of Waterloo by graduate student, Carolyn Wilson, under the

supervision of Professor Bruce Christensen, Ph.D.

Participant's name: _____   Date: _____

Participant's signature: _____   Date: _____

Witness' name: _____   Date: _____

Witness' signature: _____   Date: _____

Appendix D. The Demographic Questionnaire

Preamble to Demographic Questionnaire
(read by the graduate student before administering demographic questionnaire)

"In order to gather some general demographic information about you, I'm now going to ask you some questions about yourself. I'll be querying about such things as your age, native language, as well as your medical history. This demographic information is important to gather in this particular study as we know that certain demographic characteristics can potentially influence one's performance on the tasks that you completed as part of the study."

Demographics Questionnaire

Gender: _____

Age: _____

Race: _____

Handedness: _____

Education (program and year):
_____

Is your first language English? _____   If not, how old were you when you learned English? __

Do you wear prescription glasses or contact lenses?_____

Have you ever had difficulty in school or been diagnosed with a learning disability?
_____

Have you ever sustained a head injury? If so, under what circumstances_____

If so have you ever lost consciousness? (if so, for how long?) _____

Have you ever had an epileptic seizure or been diagnosed with a seizure disorder? _____

Have you ever had a stroke or aneurysm? _____

Have you ever had brain cancer? _____

Do you have any other major medical illness (e.g., Type I or Type II Diabetes, other cancers)?
_____

Have you ever had a psychiatric or emotional problem such as depression or anxiety?_____

Have you ever received treatment for a psychiatric or emotional problem?
_____

Have you ever received psychotherapy or counseling?_____

Have you ever been hospitalized for a psychiatric or emotion condition? _____

Have you ever received electroconvulsive shock therapy (ECT)? (if so, when and how many times?)_____

Are you currently or have you ever been on any prescription medications? (If so, specify the name of the medication, the dose, when you were on it and for how long).
_____

Does anyone in your family have a history of psychiatric or emotional problems such as depression or anxiety? (If so, specify which relative and the nature of their problem)
_____

Appendix E. Reasons for participant exclusion in study 1

High-SPQs

102: hyperthyroidism; taking Tapazole
107: computer failed to record data
110: computer failed to record data
134: history of seizures

Ave-SPQs

208: 6 PAI clinical scales with T values greater than 70 (anxiety, anxiety-related disorders, depression, paranoia, schizophrenia, borderline)
211: computer failed to record data
214: 2 PAI clinical scales with T values greater than 70 (paranoia and antisocial)
216: heart disease; has pace-maker
217: walk-in (not part of mass testing)
220: 3 PAI clinical scales with T values greater than 70 (anxiety, anxiety-related disorders, borderline)
232: 3 PAI clinical scales with T values greater than 70 (anxiety, anxiety-related disorder, borderline).
234: taking Detrol (an anti-muscarinic medication).
236: 2 PAI clinical scales with T values greater than 70 (mania, antisocial).
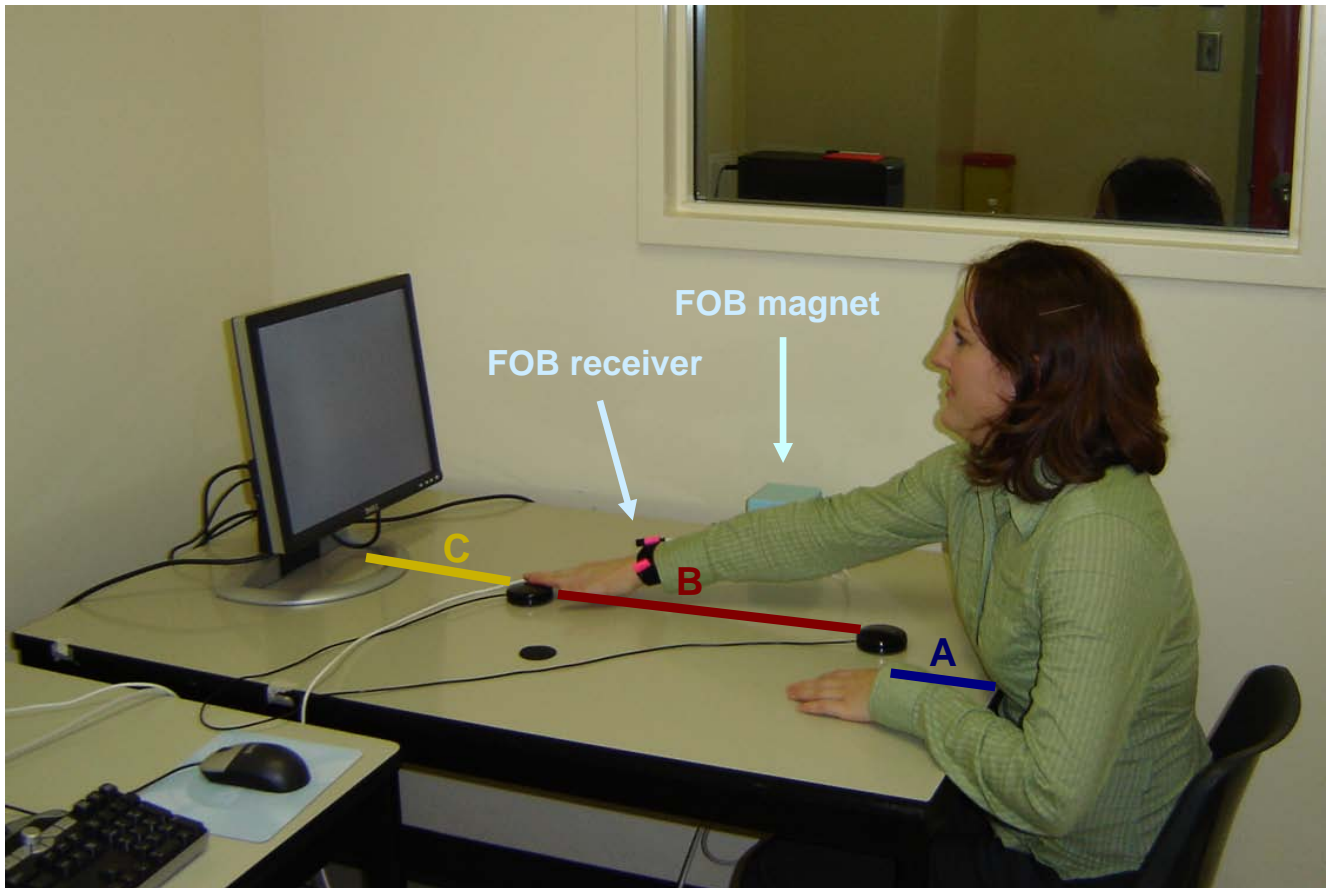
A (distance between edge of table and home key) = 17.3 cm. **B** (distance between home key and response key) = 43 cm, and **C** (distance between response key and monitor) = 21 cm.

"To start this task, place your dominant hand (i.e., the hand that you write with) on the black button closest to you (i.e., home key). Next you will see a fixation cross appear in the center of the screen. Focus on this fixation cross. The fixation cross will be followed by a green circle. As soon as you see the green circle you are to press the black button farthest away from you (i.e., response key) as quickly and accurately as possible. Sometimes the "

(presentation of 20 practice trials)

"Would you like more practice trials before we move on?" <u>Y</u>es or <u>N</u>o.

(if yes, 20 additional practice trials presented)

"Your job continues to be the same. When you see a box with a gap, press the response button as quickly and accurately as possible. However, now the computer will monitor how quickly you are responding. If you are responding fast enough, it will say, "Good!". If you need to respond faster, you will see, "Faster!". Did you have any questions before we begin?"

(experimental trials begin)

Appendix H. Task configuration

A) Configuration for trials of hiCON
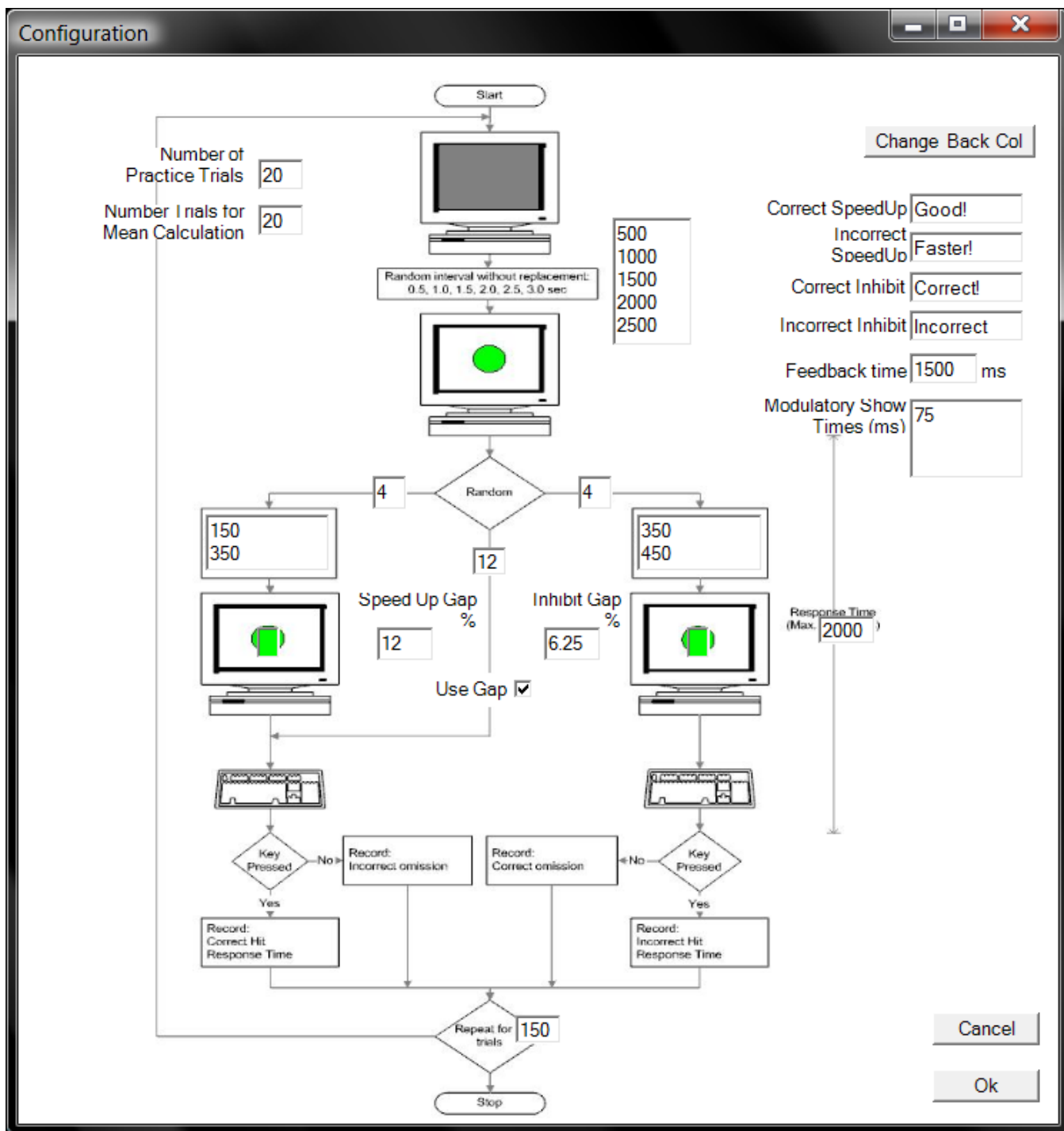
B) Configuration for Trials of loCON
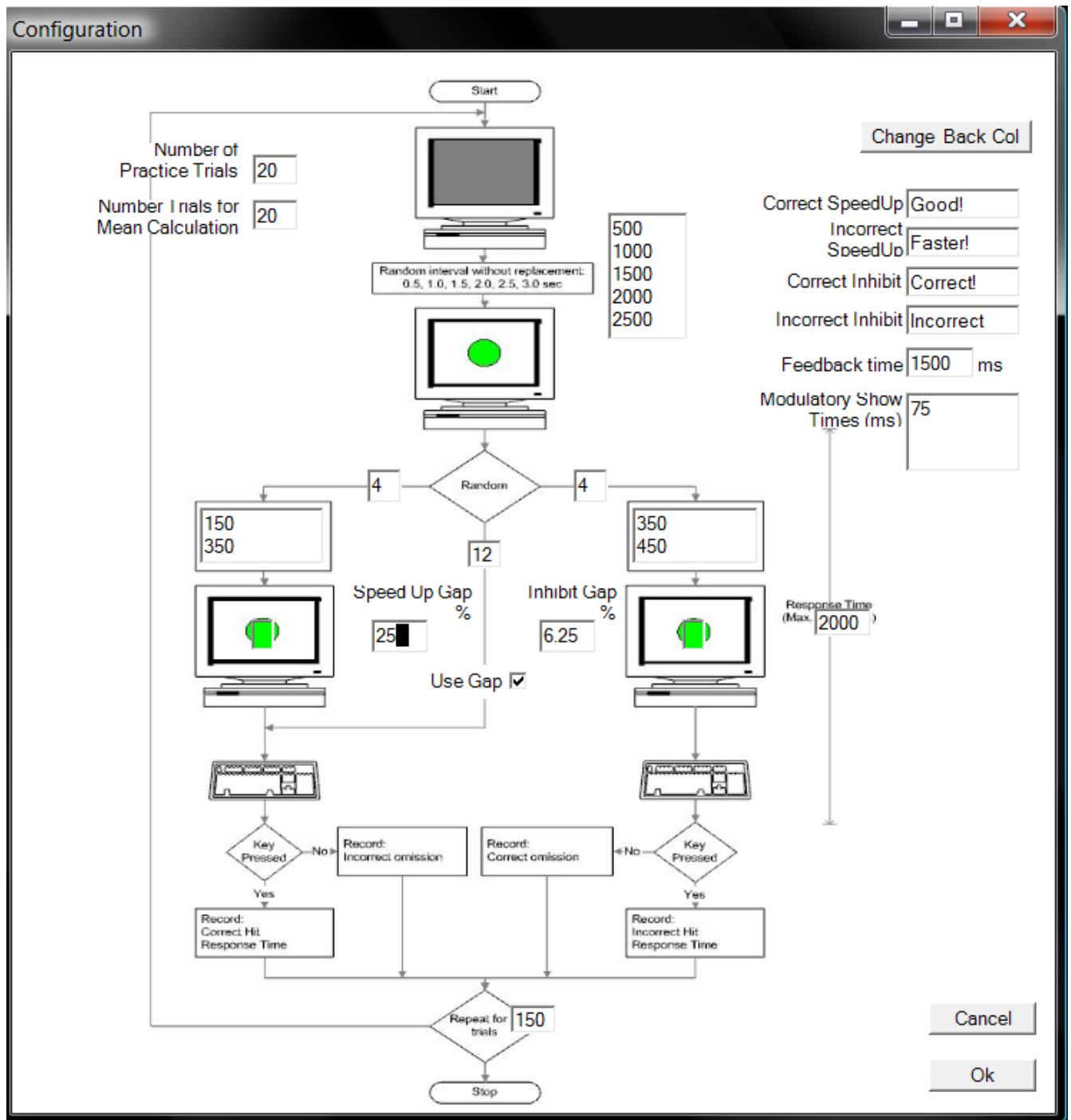
Appendix I. Protocol for assessing suicidal risk among research participants

If suicidal ideation is present, identified via either their answers' to critical items or through spontaneous disclosure, the following protocol is followed:

The study investigator will first ask whether the participant would like to be escorted to University Counseling Services in order to talk with a Counselor regarding their suicidal ideation. Specifically, the investigator will indicate that she has noticed that the participant is endorsing thoughts of suicide (as she refers to the particular items endorsed on the questionnaire) and that she would like to help facilitate the participant's contact with a mental health professional (i.e., University Counseling Services), if needed. If they agree, the participant will be escorted to Counseling Services, introduced to a Counselor, and left in their care. If, however, the participant declines this offer, the following protocol will be implemented:

The student investigator will further assess risk through the following steps:

i) Let research participant know that she (student researcher) would like to ask them additional questions about their current stressors and emotional distress
ii) Ask participant specifically about what they meant by endorsing the items that they did and why they are feeling this way
iii) Ask participant about the frequency and intensity of their suicidal thoughts
iv) Ask participant about whether they have thought of ways of harming or killing themselves (if yes, this will be followed up with questions assessing their access to methods of suicide [e.g., gun, pills])
v) Ask participant about prior suicide attempts or other self-injurious behaviour
vi) Ask participant how safe they feel being by themselves (i.e., how confident are they that they will not harm themselves)
vii) Ask the participant to comment on or rate their intention of causing self-harm

In order to assess the presence of other risk factors, the following content areas will be queried:
i) Extent and proximity of social support network
ii) Current and past drug/alcohol use
iii) Their perceived ability to problem solve and make sound decisions
iv) Whether they or their friends consider them to generally think through the consequences of their actions (or whether they are individuals who make impulsive decisions that they often regret)
v) Existence of a community mental health connection (i.e., is participant seeing a counselor, psychiatrist, etc…?)

While the participant remains in the testing room, the student researcher will consult with designated "on-call" clinical faculty member* in order to determine the participant's level of risk. If risk is determined to be moderate to high, the faculty member will speak with the participant and reiterate our desire to respond to their distress. The participant will then be

escorted to the local hospital emergency room. If the participant can safely be transported via a taxicab, the student researcher will accompany the participant in the cab to the hospital emergency room. If the participant cannot safely be transported via taxicab, ambulance or police will transport the participant. The researcher will accompany the participant until they were transferred to the care of a mental health professional (e.g., psychiatric nurse or Psychiatrist at the emergency room).

If risk is determined to be low, the designated clinical faculty member may or may not speak with the client in order to confirm level of risk. The student researcher will then convey to the participant our desire to help facilitate contact with Counseling Services or an alternate mental health professional in order to provide the participant with some psychological support. Participants will be given the phone number of Counseling Services, the Psychology Clinic, and the office phone number of the Psychologist supervising the research study. If participants are hesitant to seek counseling, the student researcher will offer to help facilitate this by phoning and making the appointment for them (with their written permission) and/or escorting them to their first appointment. The student researcher will also clarify that she will be following up with them within approximately 1 week and will confirm the phone number at which they would prefer to be contacted.

After the participant has left the study room (in the case of low risk) or is in the care of a mental health professional (in the case of moderate to high risk), the student researcher will contact her supervisor and update her on the steps taken to assess risk and subsequently intervene. If there are additional steps that the supervisor would like to be taken (e.g., examining additional questionnaire data in order to further assess suicide risk) the student researcher will do that at this time.

Some participants, based on the individual's particular circumstances, will be contacted within two weeks after participating in the study in order to follow up on 1) their mood and whether or not there has been a change in the intensity and frequency of their suicidal thinking and 2) whether they have been able to make contact with Counseling Services or an alternate mental health professional in the community. If contact has been made, and there is no imminent risk to the participant, no further contact with the research participant will be taken. If the participant has not contacted mental health services in the community, additional phone calls (e.g., 1 or 2) may be made in order to encourage contact and to monitor risk. If after additional calls, participants are not willing to seek mental health care, and they are not at imminent risk, they will not be contacted in the future. The decision to contact participants in the future would depend on a number of factors, including for example, 1) the intensity and frequency of the suicidal ideation and 2) the extent of their social supports within the community (e.g., do they have a support network of friends/family?). This decision is made in consultation with the on-call faculty member.

* when booking participants, the student researcher will arrange to have a clinical faculty member available during the last hour of the 3 hour protocol, the time during which the participants complete the questionnaires. All clinical faculty members serving in this capacity will be registered with the Ontario College of Psychologists.

Appendix J. Missing data in study 1

Participant#	Experimental condition	Variable	Group
117	loCON, lo PREP	• Peak velocity • Time at Peak Velocity • % Time at Peak Velocity	High-SPQ
	loCON, hi PREP	• Peak velocity • Time at Peak Velocity • % Time at Peak Velocity	High-SPQ
123	loCON, lo PREP	• Peak velocity • Time at Peak Velocity • % Time at Peak Velocity	High-SPQ
123	loCON, hi PREP	• Peak velocity • Time at Peak Velocity • % Time at Peak Velocity	High-SPQ
123	hiCON, lo PREP	• Peak velocity • Time at Peak Velocity • % Time at Peak Velocity	High-SPQ
123	hiCON, hi PREP	• Peak velocity • Time at Peak Velocity • % Time at Peak Velocity	High-SPQ
127	loCON, lo PREP	• Peak velocity • Time at Peak Velocity • % Time at Peak Velocity	High-SPQ
127	loCON, hi PREP	• Peak velocity • Time at Peak Velocity • % Time at Peak Velocity	High-SPQ
127	hiCON, lo PREP	• Peak velocity • Time at Peak Velocity • % Time at Peak Velocity	High-SPQ
127	hiCON, hi PREP	• Peak velocity • Time at Peak Velocity • % Time at Peak Velocity	High-SPQ
131	hiCON, lo PREP	• Peak velocity • Time at Peak Velocity • % Time at Peak Velocity	High-SPQ
131	hiCON, hi PREP	• Peak velocity • Time at Peak Velocity • % Time at Peak Velocity	High-SPQ
138	loCON, lo PREP	• Peak velocity • Time at Peak Velocity • % Time at Peak Velocity	High-SPQ

138	loCON, hi PREP	• Peak velocity • Time at Peak Velocity • % Time at Peak Velocity	High-SPQ
138	hiCON, lo PREP	• Peak velocity • Time at Peak Velocity • % Time at Peak Velocity	High-SPQ
138	hiCON, hi PREP	• Peak velocity • Time at Peak Velocity • % Time at Peak Velocity	High-SPQ
210	loCON, lo PREP	• Peak velocity • Time at Peak Velocity • % Time at Peak Velocity	Ave-SPQ
210	loCON, hi PREP	• Peak velocity • Time at Peak Velocity • % Time at Peak Velocity	Ave-SPQ
210	hiCON, lo PREP	• Peak velocity • Time at Peak Velocity • % Time at Peak Velocity	Ave-SPQ
210	hiCON, hi PREP	• Peak velocity • Time at Peak Velocity • % Time at Peak Velocity	Ave-SPQ
218	loCON, lo PREP	• Peak velocity • Time at Peak Velocity • % Time at Peak Velocity	Ave-SPQ
218	loCON, hi PREP	• Peak velocity • Time at Peak Velocity • % Time at Peak Velocity	Ave-SPQ
218	hiCON, lo PREP	• Peak velocity • Time at Peak Velocity • % Time at Peak Velocity	Ave-SPQ
218	hiCON, hi PREP	• Peak velocity • Time at Peak Velocity • % Time at Peak Velocity	Ave-SPQ
231	loCON, lo PREP	• Peak velocity • Time at Peak Velocity • % Time at Peak Velocity	Ave-SPQ
231	loCON, hi PREP	• Peak velocity • Time at Peak Velocity • % Time at Peak Velocity	Ave-SPQ
108	loCON, lo PREP	• HKRT	High-SPQ
108	loCON, hi PREP	• HKRT	High-SPQ
108	hiCON, lo PREP	• HKRT	High-SPQ
108	hiCON, hi PREP	• HKRT	High-SPQ

109	loCON, hi PREP	• HKRT	High-SPQ
109	hiCON, lo PREP	• HKRT	High-SPQ
109	hiCON, hi PREP	• HKRT	High-SPQ
111	loCON, lo PREP	• HKRT	High-SPQ
111	loCON, hi PREP	• HKRT	High-SPQ
111	hiCON, lo PREP	• HKRT	High-SPQ
111	hiCON, hi PREP	• HKRT	High-SPQ
228	loCON, lo PREP	• HKRT	Ave-SPQ
228	loCON, hi PREP	• HKRT	Ave-SPQ
228	hiCON, lo PREP	• HKRT	Ave-SPQ
228	hiCON, hi PREP	• HKRT	Ave-SPQ

loCON: low CON difficulty
hiCON: high CON difficulty
loPREP: low difficulty PREP condition
hiPREP: high difficulty PREP condition
Inh: inhibition
SU: Speed-Up
Cor: Correct
Inc: Incorrect
RT: Response Time
HKRT: Home Key Release Time

Appendix K. Skewed and kurtotic violations in study 1.

Violation	Experimental condition	Variable	Group	Z Score
Skewness	loCON, hiPREP	SU errors	High-SPQ	-3.79*
	hiCON	GoRT	Ave-SPQ	3.46*
	loCON	GoRT	Ave-SPQ	3.93**
	loCON, loPREP	SU RT_cor	Ave-SPQ	3.21*
	loCON, hiPREP	Inh HKRT_cor	High-SPQ	3.32*
	hiCON, loPREP	Inh HKRT_cor	Ave-SPQ	3.22*
	hiCON, hiPREP	Inh HKRT_cor	Ave-SPQ	4.15**
	loCON, hiPREP	Inh HKRT_cor	Ave-SPQ	4.25**
	hiCON, loPREP	SU HKRT_cor	High-SPQ	3.96*
	loCON, hiPREP	SU HKRT_cor	High-SPQ	5.22**
	loCON, loPREP	SU HKRT_cor	Ave-SPQ	3.36*
	hiCON, loPREP	SU HKRT_cor	Ave-SPQ	3.96*
	loCON, hiPREP	SU HKRT_cor	Ave-SPQ	4.54*
	hiCON, hiPREP	SU HKRT_cor	Ave-SPQ	3.96**
	hiCON, loPREP	SU PV_cor	Ave-SPQ	4.63*
	hiCON, hiPREP	SU PV_cor	Ave-SPQ	4.80*
	loCON, loPREP	SU PV_cor	Ave-SPQ	4.66*
	loCON, hiPREP	SU PV_cor	Ave-SPQ	7.35*
	hiCON, loPREP	SU TPV_cor	High-SPQ	5.34***
	hiCON, hiPREP	SU TPV_cor	High-SPQ	4.04***
	loCON, loPREP	SU TPV_cor	High-SPQ	4.30*
	loCON, hiPREP	SU TPV_cor	High-SPQ	5.05*
	hiCON, loPREP	SU TPV_cor	Ave-SPQ	3.99*
	hiCON, hiPREP	SU TPV_cor	Ave-SPQ	4.21*
	loCON, loPREP	SU TPV_cor	Ave-SPQ	3.54*
	loCON, hiPREP	SU TPV_cor	Ave-SPQ	5.49
	hiCON, loPREP	SU %TPV_cor	High-SPQ	3.46**
	hiCON, hiPREP	SU %TPV_cor	High-SPQ	4.24**
	loCON, hiPREP	SU %TPV_cor	High-SPQ	5.24**
	hiCON, loPREP	SU %TPV_cor	Ave-SPQ	3.13*
	hiCON, hiPREP	SU %TPV_cor	Ave-SPQ	4.05*
	loCON, hiPREP	SU %TPV_cor	Ave-SPQ	3.15*
Kurtosis	loCON	GORT	Ave-SPQ	3.67*
	loCON, hiPREP	Inh HKRT_cor	High-SPQ	4.35*
	hrCON, hiPREP	Inh HKRT_cor	Ave-SPQ	4.61*
	loCON, hiPREP	Inh HKRT_cor	Ave-SPQ	5.77**
	hiCON, loPREP	SU HKRT_cor	High-SPQ	6.65****
	loCON, hiPREP	SU HKRT_cor	High-SPQ	7.59
	loCON, hiPREP	SU HKRT_cor	Ave-SPQ	7.36
	hiCON, loPREP	SU PV_cor	Ave-SPQ	5.74*

hiCON, hiPREP	SU PV_cor	Ave-SPQ	5.31*
loCON, loPREP	SU PV_cor	Ave-SPQ	5.63*
loCON, hiPREP	SU PV_cor	Ave-SPQ	13.04*
hiCON, loPREP	SU TPV_cor	High-SPQ	8.08
loCON, loPREP	SU TPV_cor	High-SPQ	4.08*
loCON, hiPREP	SU TPV_cor	High-SPQ	7.50
hiCON, loPREP	SU TPV_cor	Ave-SPQ	6.25
hiCON, hiPREP	SU TPV_cor	Ave-SPQ	3.68*
loCON, loPREP	SU TPV_cor	Ave-SPQ	3.81*
loCON, hiPREP	SU TPV_cor	Ave-SPQ	9.33
hiCON, hiPREP	SU %TPV_cor	High-SPQ	3.66**
loCON, hiPREP	SU %TPV_cor	High-SPQ	5.59**
hiCON, loPREP	SU %TPV_cor	Ave-SPQ	12.26*
loCON, hiPREP	SU %TPV_cor	Ave-SPQ	4.09*

* squareroot transformation able to normalize distribution
**log transformation able to normalize distribution
***inverse
****cosine
loCON: low CON difficulty
hiCON: high CON difficulty
loPREP: low difficulty PREP condition
hiPREP: high difficulty PREP condition
Inh: inhibition
SU: Speed-Up
Cor: Correct
Inc: Incorrect
RT: Response Time
HKRT: Home Key Release Time
PV: Peak velocity
TPV: Time to Peak Velocity
PTPV: Percent Time to Peak Velocity

Appendix L. Univariate outliers in study 1.

Violation	Participant#	Experimental condition	Variable	Group	Z Score
Outliers	221	loCON, hiPREP	Inh Errors	Ave-SPQ	3.73
	240	loCON, hiPREP	SU Errors	Ave-SPQ	-3.13
	240	hiCON, hiPREP	SU Errors	Ave-SPQ	-3.15
	240	loCON	GoRT	Ave-SPQ	3.40
	215	loCON, loPREP	SU RT_cor	Ave-SPQ	3.21
	123	hiCON, loPREP	SU RT_inc	High-SPQ	4.167
	115	loCON, loPREP	Inh HKRT_cor	High-SPQ	4.08
	104	loCON, hiPREP	Inh HKRT_cor	High-SPQ	3.95
	215	loCON, hiPREP	Inh HKRT_cor	Ave-SPQ	3.36
	231	hiCON, hiPREP	Inh HKRT_cor	Ave-SPQ	3.25
	112	hiCON, loPREP	Inh HKRT_inc	High-SPQ	3.50
	130	hiCON, hiPREP	Inh HKRT_inc	High-SPQ	4.24
	112	loCON, hiPREP	Inh HKRT_inc	High-SPQ	4.64
	128	hiCON, loPREP	SU HKRT_cor	High-SPQ	3.48
	130	loCON, hiPREP	SU HKRT_cor	High-SPQ	3.22
	130	hiCON, hiPREP	SU HKRT_cor	High-SPQ	3.63
	112	loCON, hiPREP	SU HKRT_inc	High-SPQ	3.15
	131	hiCON, hiPREP	SU HKRT_inc	High-SPQ	3.35
	108	hiCON, loPREP	SU PV_cor	High-SPQ	3.15
	135	loCON, hiPREP	SU PV_cor	High-SPQ	4.04
	118	hiCON, loPREP	SU PV_inc	High-SPQ	3.06
	135	loCON, hiPREP	SU PV_inc	High-SPQ	4.44
	133	hiCON, loPREP	SU TPV_cor	High-SPQ	3.34
	112	loCON, hiPREP	SU TPV_cor	High-SPQ	3.84
	222	hiCON, loPREP	SU TPV_cor	Ave-SPQ	3.33
	237	hiCON, hiPREP	SU TPV_cor	Ave-SPQ	3.42
	201	loCON, loPREP	SU TPV_cor	Ave-SPQ	3.52
	222	loCON, hiPREP	SU TPV_cor	Ave-SPQ	4.22
	242	hiCON, loPREP	SU TPV_inc	Ave-SPQ	3.18
	222	hiCON, hiPREP	SU TPV_inc	Ave-SPQ	4.02
	201	loCON, loPREP	SU TPV_inc	Ave-SPQ	3.23
	222	loCON, hiPREP	SU TPV_inc	Ave-SPQ	4.38
	129	hiCON, hiPREP	SU TPV_inc	High-SPQ	3.08
	133	loCON, loPREP	SU TPV_inc	High-SPQ	3.26
	130	loCON, hiPREP	SU TPV_inc	High-SPQ	3.27
	139	hiCON, loPREP	SU PTPV_cor	High-SPQ	-3.12
	222	hiCON, loPREP	SU PTPV_cor	Ave-SPQ	-4.05
	222	hiCON, hiPREP	SU PTPV_cor	Ave-SPQ	-3.57
	121	hiCON, loPREP	SU PTPV_inc	High-SPQ	4.62
	112	hiCON, hiPREP	SU PTPV_inc	High-SPQ	3.54
	222	hiCON, hiPREP	SU PTPV_inc	Ave-SPQ	4.62

| 222 | loCON, loPREP | SU PTPV_inc | Ave-SPQ | 3.14 |
| 222 | loCON, hiPREP | SU PTPV_inc | Ave-SPQ | 4.24 |

loCON: low CON difficulty
hiCON: high CON difficulty
loPREP: low difficulty PREP condition
hiPREP: high difficulty PREP condition
Inh: inhibition
SU: Speed-Up
Cor: Correct
Inc: Incorrect
RT: Response Time
HKRT: Home Key Release Time
PV: Peak velocity
TPV: Time to Peak Velocity
PTPV: Percent Time to Peak Velocity

Appendix M. Response time (RT) on incorrect SU trials in study 1.

Analyses were also undertaken in order to examine trials involving unsuccessful attempts of participants to speed-up their responses. Of note, this analysis excludes any SU trials in which the participant fails to make a response (i.e., on trials in which participants incorrectly interpret the SU signal as an INH signal). Analyses were conducted on data from 34/37 High-SPQs and from 28/32 Ave-SPQs. A main effect of PREP (F [1, 60] = 83.678, p < .001) was observed, with participants showing longer RTs on trials of hiPREP difficulty vs. low PREP difficulty. A main effect of CON was also observed (F [1, 60] = 39.752, p < .001), with participants showing longer RTs when CON difficulty was high. A trend towards a PREP X CON X Group interaction (F [1, 60] = 3.874, p =.054) was also observed. Simple effects testing showed that across incorrect SU trials (i.e., when participants were not able to increase their response time after seeing the SU signal, relative to the previous 10 Go trials), Ave-SPQs, but not High-SPQs, had marginally longer SURTs times only in loPREP, hiCON conditions , t (1, 46.072) = -2.366, p=.022). No main effect of group (F [1, 60] = 3.140, p=.081) was observed.

Appendix N. Clinical correlates of AIT#1 experimental variables from study 1.

Clinical Measure	Subscale or Factor Score	Experimental Correlate	Experimental Condition	Correlation Coefficient (r)	P Value
SPQ	Disorganized	hiPREP, hiCON	SURT	r =.- 245	p=.43
	Interpersonal	hiPREP, hiCON	SU HKRT	r =-.272	p=.037
	OEB	loPREP, loCON	INH error	r =. 244	p=.043
	ESA	hiPREP, loCON	INH error	r =-.310	p=.010
	NCF	hiPREP, loCON	INH error	r =-.283	p=.019
	NCF	loPREP, hiCON	SU error	r =.265	p=.028
	NCF	hiPREP, hiCON	SURT	r =-.258	p=.048
	CA	hiPREP, loCON	INH error	r =-.314	p=.009
	OB/MT	loPREP, hiCON	INH error	r =.334	p=.005
	SUS	hiPREP, hiCON	SURT	r =-.239	p=.048
	SUS	hiPREP, hiCON	SU HKRT	r =.311	p=.017
	OEB	loPREP, loCON	INH HKRT	r =.280	p=.020
PAI	SCZ	loPREP, loCON	INH error	r =.293	p=.013
	BOR	loPREP, loCON	INH error	r =.271	p=.024
	ANT	loPREP, loCON	INH error	r =.308	p=.024
	AGG	loPREP, loCON	INH error	r =.375	p=.002
	SUI	loPREP, loCON	INH error	r =.242	p=.045
	DRG	loPREP, hiCON	INH error	r =.243	p=.028
	DRG	hiPREP, loCON	INH error	r =.265	p=.028
	DRG	hiPREP, hiCON	INH error	r =.281	p=.019
	AGG	hiPREP, loCON	INH error	r =.383	p=.001
	AGG	hiPREP, hiCON	INH error	r =.264	p=.029
	DRG	loPREP, loCON	SU error	r =.257	p=.037
	ARD	hiPREP, loCON	SU error	r =.251	p=.037
	PAR	loPREP, loCON	SURT	r =-.297	p=.015
	PAR	loPREP, loCON	SURT	r =-.280	p=.022
	ANT	loPREP, loCON	SURT	r =-.276	p=.024
	BOR	loPREP, loCON	SURT	r =-.278	p=.023
	BOR	hiPREP, hiCON	SURT	r =-.255	p=.037
	AGG	loPREP, loCON	SURT	r =.271	p=.025
	AGG	hiPREP, hiCON	SURT	r =-.295	p=.016
	AGG	loPREP, loCON	SURT	r =-.339	p=.005
	SCZ	loPREP, loCON	INH HKRT	r =.246	p=.046
	ANT	hiPREP, hiCON	INH HKRT	r =.297	p=.014
	ARD	loPREP, hiCON	INH HKRT	r =-.243	p=.049
	DEP	loPREP, loCON	INH HKRT	r =.261	p=.033
	PAR	loPREP, hiCON	INH HKRT	r =-.250	p=.043
	PAR	loPREP, hiCON	SU HKRT	r =-.261	p=.040
	PAR	hiPREP, hiCON	SU HKRT	r =-.291	p=.028
	ARD	hiPREP, loCON	SU HKRT	r =-.261	p=.034
	BOR	loPREP, loCON	SU HKRT	r =-.270	p=.034
NEO-FFI	Openness to	loPREP, loCON	INH error	r =.246	p=.041

	Experience Openness to Experience	loPREP, hiCON	INH error	r =.265	p=.028
	Openness to Experience	hiPREP, hiCON	INH error	r =.259	p=.032
	Agreeableness	hiPREP, hiCON	INH error	r =-.274	p=.023
	Openness to Exp	loPREP, loCON	SU error	r =.257	p=.033
	Openness to Exp	hiPREP, hiCON	SU error	r =-.280	p=.020
WAIS-III	Estimated FSIQ	loPREP, hiCON	INH HKRT	r =.365	p=.002
	Estimated FSIQ	loPREP, loCON	SU HKRT	r =.281	p=.020

Schizotypal Personality Questionnaire (SPQ):

Factors: COG-PER: Cognitive Perceptual Factor, INT: Interpersonal, DIS: Disorganized

Subscales: IOR: ideas of reference, ESA: excessive Social Anxiety, OB/MG: odd behaviour/magical thinking, UPE: unusual perceptual experiences, OEB: odd/eccentric behaviour, NCF: no close friends,

OS: odd speech, CA: constricted affect, S: suspiciousness.

PAI subscales:

SOM: Somatic Complaints, ANX: Anxiety, ARD: Anxiety-Related Disorders, DEP: Depression, MAN: Mania, PAR: Paranoia, SCZ: Schizophrenia, BOR: Borderline, ANT: Antisocial Features, DRG: Drug Problems, ALC: Alcohol Problems, AGG: Aggression, SUI: Suicidal Ideation, NS: Nonsupport, TR: Treatment Rejection, DOM: Dominance, WAR: Warmth.

loCON: low CON difficulty
hiCON: high CON difficulty
loPREP: low difficulty PREP condition
hiPREP: high difficulty PREP condition
Go error: error (of omission) on Go Trial
GoRT: Response Time on Go Trials
GoHKRT: HKRT on Go Trial
HKRT: Home Key Release Time
NoGo error: error (of commission) on NoGo Trial
NoGoHKRT: HKRT on NoGo Trial

Appendix O. Description of Study 2 for psychology department recruitment website

The Personality and Motor Skills study involves examining the relationship between personality dimensions and motor skill. The experiment will take about 3 hours of your time, and you will receive 3 credits for your participation. The experiment involves completing some tasks on the computer that have been designed to examine your speed and accuracy in responding to cognitive stimuli. Specifically, we are interested in how certain personality features, such as creativity, relate to your performance on these tasks. As part of the study we will also be asking you to complete various questionnaires, some of which ask about potentially sensitive topics such as whether you have a history of psychological trauma or a history of mental illness. Importantly, all information disclosed during the study is confidential. Participation in the study also involves providing a DNA sample. Research suggests that personality features such as creativity and openness to experience have a genetic basis. In examining your DNA, as it relates to the presence of certain personality features, we aim to gain a better understanding of the biological underpinnings of personality. To obtain a sample of your DNA, you will be given a soft-bristled brush and asked to brush it against the inside of your cheek. Cells from your cheek will adhere to the brush. You will then pass the brush to the researcher who will place it in a container that identifies the sample only by a number code. Your name will <u>not</u> be on the sample. Once the analyses are completed, the sample will be destroyed.

Appendix P. Cover sheet, consent forms, and debriefing/education feedback forms for study 2

Title of Project: Personality and Motor Skills

Principal Investigator: Dr. Bruce Christensen
                            Department of Psychology
                            University of Waterloo
                            Office Telephone: (416) 535-8501, ext. 6843
                            Email: Bruce_Christensen@camh.net

Student Investigator: Carolyn Wilson
                            Department of Psychology
                            University of Waterloo
                            Email:cmwilson@watarts.uwaterloo.ca

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Directions

Attached to this introduction is a detailed Consent Form that outlines the purpose of the experiment and your rights as a research participant. If you are still interested in participating in this project after reading the materials, please sign both copies of the consent form and keep one for your own records. The experiment will proceed in the following manner.

6.   You will first be given an opportunity to wash your hands.

7.   Next, you will be asked to wash your mouth out with water (provided in a sealed bottle) and given a new packaged toothbrush to brush gently against the inside of your cheek.

8.   We will then get you to wash your mouth out with water again.

9.   After this, we will provide you with a new packaged brush that you will use to gently brush against the inner surface of your cheek. Cells from your cheek will adhere to the brush.

10.   You will then pass the brush to the researcher who will place it in a sterile container that identifies the sample only by a number code, and again be given an opportunity to wash your hands.

11.   You will then be asked to complete a series of computer tasks that test speed and accuracy of motor responses to cognitive stimuli.

12.   Next, you will be required to complete a questionnaire that asks you for various demographic details about yourself such as age, native language, and medical history.

13.   Next, you will complete a series of questionnaires enquiring about your current feelings, thoughts, and behaviour.

14.   Next, you will complete a few tasks testing your general knowledge and problem-solving abilities.

> ❖ **In order to ensure confidentiality, please <u>DO NOT</u> record your name anywhere on the questionnaire.**
>
> ❖ **Please read each question carefully and make a quick decision as to which response best describes you.**

15.   At the end of the study, you will be fully debriefed and provided with an educational feedback form. Additionally, you will be given the opportunity to ask the research assistant or graduate student any questions that you might have.

Thank you in advance for your assistance with this project.

If you have any questions about the experiment, please ask the experimenter now before proceeding any further with the study.

Title of Project: Personality and Motor Skills

Principal Investigator: Dr. Bruce Christensen
                    Department of Psychology
                    University of Waterloo
                    Office Telephone: (416) 535-8501, ext. 6843
                    Email: Bruce_Christensen@camh.net

Student Investigators: Carolyn Wilson
                    Department of Psychology
                    University of Waterloo
                    Email:cmwilson@watarts.uwaterloo.ca

You are invited to participate in an experiment that involves completing some tasks on the computer that have been designed to examine your speed and accuracy in responding to cognitive stimuli. You will also complete a questionnaire that asks for various demographic details about yourself such age, native language, and medical history. In addition, you will also complete a series of paper and pencil questionnaires that ask you about your thoughts, feelings, and behaviour. Specifically, we are interested in how certain personality features, such as creativity, relate to your performance on these tasks. Your participation in this study also involves providing a DNA sample. To obtain the sample, you will first be given an opportunity to wash your hands. Next, you will be asked to wash your mouth out with water (provided in a sealed bottle) and given a new packaged toothbrush to brush gently against the inside of your cheek. We will then get you to wash your mouth out with water again. After this, we will provide you with a new packaged brush that you will use to gently brush against the inner surface of your cheek. Cells from your cheek will adhere to the brush. You will then pass the brush to the researcher who will place it in a sterile container that identifies the sample only by a number code. This code will ensure that the results of the DNA analysis are accurately linked to each participant's questionnaire results. However, participants' names will not be on the sample. An analysis of the DNA will be conducted by a research colleague at the University of Toronto, Dr. Albert Wong. Once the analyses are completed, the sample will be destroyed by the researcher".

Participation in this study is voluntary. The study will take approximately 2.5-hours and you will receive 2 participation credits for your time.

By volunteering in the present project, you will learn more about psychological research in general, and the topics of this study in particular (i.e., personality features and motor skills). At the end of the study you will be provided with a detailed feedback sheet outlining the research project. There are no physical risks to participating in the study. However, you may experience some degree of frustration while carrying out the computer tasks.

You are free to withdraw from the study at any point without penalty or loss of money earned up until that point in the study. If you would like to discontinue, simply inform the individual conducting the experiment (i.e., research assistant or graduate student). You may decline to carry out any of the tasks involved in the study. All the information you provide will be kept strictly confidential. Your name and/or student ID number will not be associated with any of the research materials. Consent forms will be stored separately from the questionnaire and experimental data so your identity cannot be matched

with your responses in the experiment. Consent forms will also be stored separately from the DNA samples. In accordance with the Canadian Psychological Association research guidelines, the raw data will be stored in a locked room for seven years after completion of the study, at which point it will be destroyed. In accordance with guidelines when dealing with human specimens, DNA samples will be destroyed at the conclusion of analyses. Only individuals authorized by Dr. Christensen will have access to the data during this period.

This study has been reviewed by and has received ethics clearance from the UW Office of Research Ethics. If you have any concerns about your participation in this study, you may contact Dr. Susan Sykes, Director of the Office of Research Ethics (888-4567, ext. 6005). If you have questions or concerns about the study itself or your reaction to it, you may discuss them with the student investigator, Carolyn Wilson (cmwilson@watarts.uwaterloo.ca) or with the principal investigator and faculty supervisor, Dr. Bruce Christensen ([416] 535-8501, ext. 6843; Bruce_Christensen@camh.net). Dr. Christensen is a licensed psychologist who specializes in the assessment and research of cognitive functioning. You may also contact UW Counseling Services at 888-4567, ext. 2655 if you feel you may need ongoing assistance with any personal difficulties.

Thank you for your assistance in this project.

I agree to participate in a study conducted by Bruce Christensen and Carolyn Wilson on personality and motor skills. I have made this decision based on the information I have read in the Introductory Sheet and Consent Form and have had all my questions about participating in the experiment addressed by the experimenter. I understand that I may withdraw this consent at any time by declaring this intention to the experimenter. I realize that I will not incur any penalty or lose my participation credits for withdrawing my consent. I also understand that this project has been evaluated by and received ethics clearance from the UW Office of Research Ethics. If I have any concerns about this study I can contact Dr. Susan Sykes, Director of the UW Office of Research Ethics at 888-4567, ext. 6005

If you are willing to participate in this experiment, please sign both copies of the Consent Form and keep one copy for your records.

Participant's Name (please print):   _____
Participant's Signature: _____
Date: _____

Witness' Name (please print):   _____
Witness' Signature: _____
Date: _____

Title of Project: Personality and Motor Skills

Principal Investigator: Dr. Bruce Christensen
                          Department of Psychology
                          University of Waterloo
                          Office Telephone: (416) 535-8501, ext. 6843
                          Email: Bruce_Christensen@camh.net

Student Investigators: Carolyn Wilson
                          Department of Psychology
                          University of Waterloo
                          Email:cmwilson@watarts.uwaterloo.ca

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You are invited to participate in an experiment that involves completing some tasks on the computer that have been designed to examine your speed and accuracy in responding to cognitive stimuli. You will also complete a questionnaire that asks for various demographic details about yourself such age, native language, and medical history. In addition, you will also complete a series of paper and pencil questionnaires that ask you about your thoughts, feelings, and behaviour. Specifically, we are interested in how certain personality features, such as creativity, relate to your performance on these tasks. Your participation in this study also involves providing a DNA sample. To obtain the sample, you will first be given an opportunity to wash your hands. Next, you will be asked to wash your mouth out with water (provided in a sealed bottle) and given a new packaged toothbrush to brush gently against the inside of your cheek. We will then get you to wash your mouth out with water again. After this, we will provide you with a new packaged brush that you will use to gently brush against the inner surface of your cheek. Cells from your cheek will adhere to the brush. You will then pass the brush to the researcher who will place it in a sterile container that identifieds the sample only by a number code. This code will ensure that the results of the DNA analysis are accurately linked to each participant's questionnaire results. However, participants' names will not be on the sample. An analysis of the DNA will be conducted by a research colleague at the University of Toronto, Dr. Albert Wong. Once the analyses are completed, the sample will be destroyed by the researcher".
  Participation in this study is voluntary. The study will take approximately 2.5-hours and you will receive $8 per hour for your time.

By volunteering in the present project, you will learn more about psychological research in general, and the topics of this study in particular (i.e., personality features and motor skills). At the end of the study you will be provided with a detailed feedback sheet outlining the research project. There are no physical risks to participating in the study. However, you may experience some degree of frustration while carrying out the computer tasks.

You are free to withdraw from the study at any point without penalty or loss of money earned up until that point in the study. If you would like to discontinue, simply inform the individual conducting the experiment (i.e., research assistant or graduate student). You may decline to carry out any of the tasks involved in the study. All the information you provide will be kept strictly confidential. Your name and/or student ID number will not be associated with any of the research materials. Consent forms will be stored separately from the questionnaire and experimental data so your identity cannot be matched with your responses in the experiment. Consent forms will also be stored separately from the DNA

samples. In accordance with the Canadian Psychological Association research guidelines, the raw data will be stored in a locked room for seven years after completion of the study, at which point it will be destroyed. In accordance with guidelines when dealing with human specimens, DNA samples will be destroyed at the conclusion of analyses. Only individuals authorized by Dr. Christensen will have access to the data during this period.

This study has been reviewed by and has received ethics clearance from the UW Office of Research Ethics. If you have any concerns about your participation in this study, you may contact Dr. Susan Sykes, Director of the Office of Research Ethics (888-4567, ext. 6005). If you have questions or concerns about the study itself or your reaction to it, you may discuss them with the student investigator, Carolyn Wilson (cmwilson@watarts.uwaterloo.ca) or with the principal investigator and faculty supervisor, Dr. Bruce Christensen ([416] 535-8501, ext. 6843; Bruce_Christensen@camh.net). Dr. Christensen is a licensed psychologist who specializes in the assessment and research of cognitive functioning. You may also contact UW Counseling Services at 888-4567, ext. 2655 if you feel you may need ongoing assistance with any personal difficulties.

Thank you for your assistance in this project.

I agree to participate in a study conducted by Bruce Christensen and Carolyn Wilson on personality and motor skills. I have made this decision based on the information I have read in the Introductory Sheet and Consent Form and have had all my questions about participating in the experiment addressed by the experimenter. I understand that I may withdraw this consent at any time by declaring this intention to the experimenter. I realize that I will not incur any penalty or lose my participation credits for withdrawing my consent. I also understand that this project has been evaluated by and received ethics clearance from the UW Office of Research Ethics. If I have any concerns about this study I can contact Dr. Susan Sykes, Director of the UW Office of Research Ethics at 888-4567, ext. 6005

If you are willing to participate in this experiment, please sign both copies of the Consent Form and keep one copy for your records.

Participant's Name (please print):   _____

Participant's Signature: _____

Date: _____

Witness' Name (please print):   _____

Witness' Signature: _____

Date: _____

Title of Project: Personality and Motor Skills

Principal Investigator: Dr. Bruce Christensen
Department of Psychology
University of Waterloo
Office Telephone: (416) 535-8501, ext. 6843
Email: Bruce_Christensen@camh.net

Student Investigators: Carolyn Wilson
Department of Psychology
University of Waterloo
Email:cmwilson@watarts.uwaterloo.ca

In the present study we asked you to complete a number of computer tasks, as well as a series of questionnaires. The primary focus of the project was to refine novel tasks used to examine how certain personality features, such as openness to experience and creativity, relate to motor skills such as velocity and accuracy of movement.

We know that people who share these types of personality features can often be very sensitive to emotional stimuli. By looking at your motor responses to emotional stimuli, such as the pictures you viewed on the computer screen, we aimed to further develop this objective measure of your responses to such stimuli. Additionally, by obtaining a DNA sample from you we hope to gain a better understanding of the molecular bases of these personality features.

We also know that these personality features can influence how we organize information and solve problems. By examining your motor responses to the different stimuli that appeared on the computer screen, we aimed to investigate measures that could accurately depict the association between personality dimensions and your problem-solving abilities.

The questionnaire that you completed was used to enable us to further characterize your current feelings, thoughts, and experiences.

Consent forms will be stored separately from the DNA samples in order to ensure your continued confidentiality. In accordance with guidelines when dealing with human specimens, DNA samples will be destroyed at the conclusion of study.

Thank you for your participation in the current study. Your efforts are greatly appreciated.

If you have any questions or concerns about this study, please feel free to contact Carolyn Wilson (cmwilson@watarts.uwaterloo.ca) or Dr. Bruce Christensen Bruce_Christensen@camh.net; 888-4567, ext. 3052). Dr. Christensen is a licensed Psychologist who specializes in understanding cognitive processes in various clinical populations.

If you feel at all concerned about the items on the questionnaire you completed during the experiment, please contact Dr. Christensen. You may also wish to contact UW Counseling Services (888-4567, ext. 2655). More generally, if you have any concerns about your participation in this study you may contact Dr. Susan Sykes, who is the Director of the UW Office of Research Ethics (888-4567, ext. 6005).

References:

Kleinsorge, T. (2001). The time course of effort mobilization and strategic adjustments of response criteria. *Psychological Research*, *65,* 216 – 223.

Rothermund, K., Wentura, D., & Bak, P.M. (2001). Automatic attention to stimuli signaling chances and dangers: moderating effects of positive and negative goal and action contexts. *Cognition and Emotion, 15 (2*), 231 – 248.

Personality and Motor Skills Study Payment Record Form

This hereby certifies that _____

received $_____ for his/her involvement in the Personality and Motor Skills Study conducted at The

University of Waterloo by graduate student, Carolyn Wilson, under the supervision of Professor Bruce

Christensen, Ph.D.

Participant's name: _____   Date: _____

Participant's signature: _____   Date: _____

Witness' name: _____   Date: _____

Witness' signature: _____   Date: _____

Appendix Q. Reasons for participant exclusion in study 2

<u>High-SPQs</u>
125: epilepsy

<u>Ave-SPQs</u>

206: PAI Depression scale: T=72; PAI Borderline scale: T=79
209: PAI Borderline scale: T=73
210: PAI Paranoia scale: T=71, Borderline scale: T=76
212: History of seizures. Seizure meds for 2 years (when 9 – 11 y.o.)
216: PAI Depression scale: T=72; Schizophrenia scale: T=72; Borderline scale: T=79
218: PAI Borderline scale: T=71
226: PAI Anxiety Related Disorders scale: T=70
241: Brain surgery for blood clots when 2 y.o.

Appendix R. AIT-R instructions

"To start this task, place your dominant hand (i.e., the hand that you write with) on the black button closest to you (i.e., home key). Next you will see a fixation cross appear in the center of the screen. Focus on this fixation cross. The fixation cross will be followed by the word, "GO". When you see the word "GO" your job is to press the response button as quickly and accurately as possible. Did you have any questions before we begin the practice trials?"

(presentation of 20 practice trials)

"Would you like more practice trials before we move on?" <u>Y</u>es or <u>N</u>o.

(if yes, 20 additional practice trials presented)

"Your job continues to be the same. When you see a box with a gap, press the response button as quickly and accurately as possible.

However, now the computer will monitor how quickly you are responding. If you are responding fast enough, it will say, "Good!". If you need to respond faster, you will see, "Faster!". Did you have any questions before we begin?"

(experimental trials begin)

Appendix S. Schematic of AIT-R configuration

i) HiPREP, HiCON Condition.
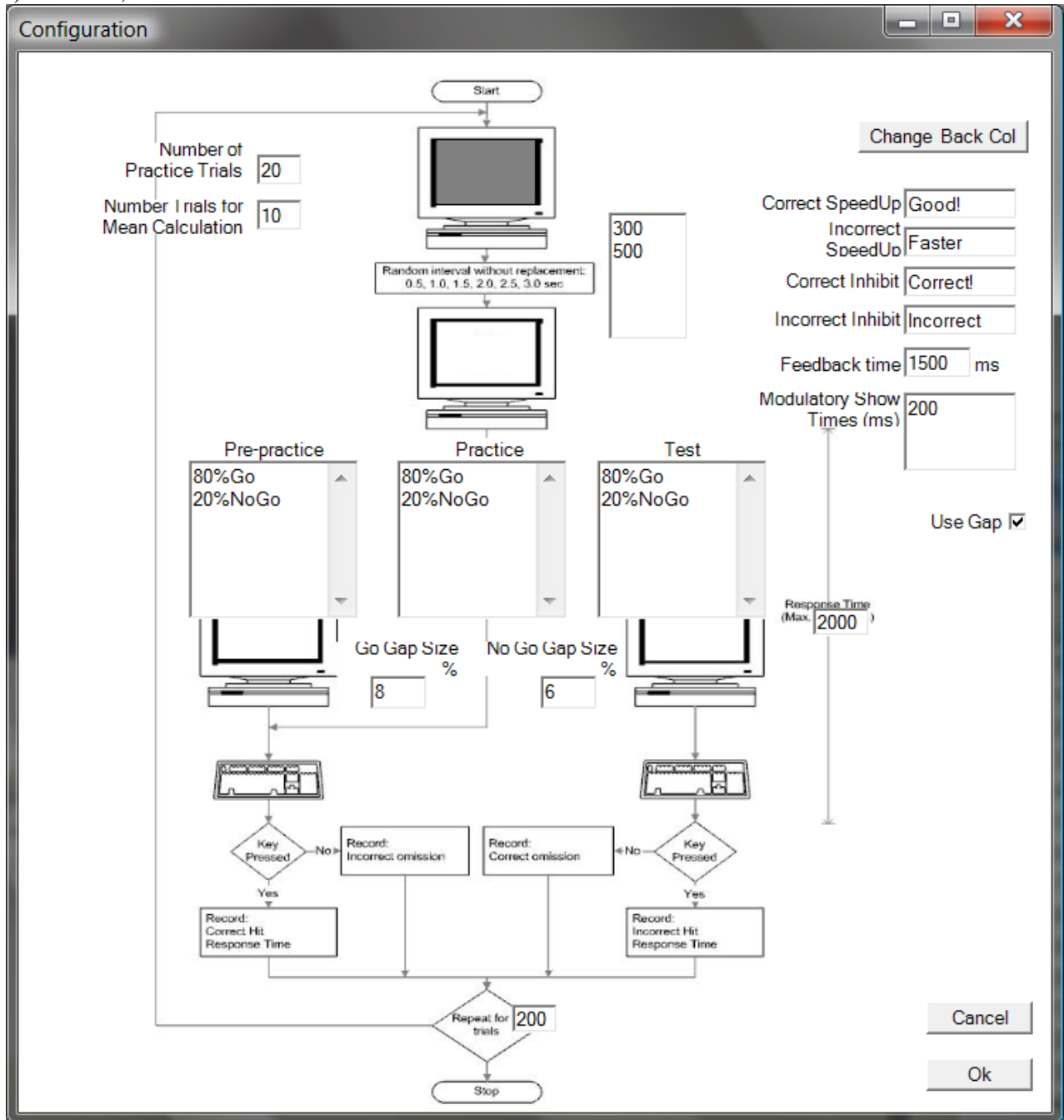
ii) LoPREP, HiCON Condition.

iii: HiPREP, LoCON Condition.

Configuration

Start

Number of
Practice Trials 20

Number Trials for
Mean Calculation 10

Change Back Col

Correct SpeedUp Good!
Incorrect
SpeedUp Faster

Correct Inhibit Correct!

Incorrect Inhibit Incorrect

Feedback time 1500 ms

Modulatory Show
Times (ms) 75

300
500

Random interval without replacement:
0.5, 1.0, 1.5, 2.0, 2.5, 3.0 sec

Pre-practice   Practice   Test
80%Go   80%Go   80%Go
20%NoGo   20%NoGo   20%NoGo

Use Gap ☑

Go Gap Size   No Go Gap Size
%   %
10   6

Response Time
(Max. 2000)

Key
Pressed   No ▶ Record:
                Incorrect omission

Record:
Correct omission ◀ No   Key
                         Pressed

Yes   Yes

Record:
Correct Hit
Response Time

Record:
Incorrect Hit
Response Time

Repeat for 200
trials

Cancel

Ok

Stop

iv: LoPREP, LoCON Condition.

Appendix T. Missing experimental data in study 2

Participant#	Experimental condition	Variable	Group
106	ALL	• Mean GoRT	High-SPQ
		• Mean Go HKRT_Cor	High-SPQ
		• Mean Go HKRT_Inc	High-SPQ
		• Mean NoGo HKRT_Cor	High-SPQ
		• % NoGo HKR_Cor	High-SPQ
		• Go error rate	High-SPQ
		• NoGo error rate	High-SPQ
213	ALL	• Mean GoRT	Ave-SPQ
		• Mean Go HKRT_Cor	Ave-SPQ
		• Mean NoGo HKRT_Cor	Ave-SPQ
		• % NoGo HKR_Cor	Ave-SPQ
		• Go error rate	Ave-SPQ
		• NoGo error rate	Ave-SPQ
214	ALL	• Mean GoRT	Ave-SPQ
		• Mean Go HKRT_Cor	Ave-SPQ
		• Mean NoGo HKRT_Cor	Ave-SPQ
		• % NoGo HKR_Cor	Ave-SPQ
		• Go error rate	Ave-SPQ
		• NoGo error rate	Ave-SPQ

Appendix U. Univariate outliers in study 2.

Violation	Part.#	Experimental condition	Variable	Group	Z Score
Outlier	146	loPREP, loCON	RT	High-SPQ	-3.232
	101	loPREP, loCON	GoHKRT_Cor	High-SPQ	-4.366
	113	hiPREP, hiCON	GoHKRT_Cor	High-SPQ	-3.074
	101	loPREP, loCON	HKRT_NoGo_Cor	High-SPQ	-4.529
	101	loPREP, hiCON	HKRT_NoGo_Cor	High-SPQ	-3.560
	113	loPREP, hiCON	HKRT_NoGo_Cor	High-SPQ	-3.273
	101	hiPREP, loCON	HKRT_NoGo_Cor	High-SPQ	-3.859
	101	hiPREP, hiCON	HKRT_NoGo_Cor	High-SPQ	-3.590
	109	loPREP, loCON	Go errors	High-SPQ	-3.442
	148	loPREP, loCON	Go errors	High-SPQ	4.053
	132	loPREP, hiCON	Go errors	High-SPQ	3.129
	147	loPREP, hiCON	Go errors	High-SPQ	3.712
	109	hiPREP, loCON	Go errors	High-SPQ	5.720
	109	hiPREP, hiCON	Go errors	High-SPQ	3.552
	132	hiPREP, hiCON	Go errors	High-SPQ	4.814
	146	loPREP, loPREP	NoGo errors	High-SPQ	3.895
	130	loPREP, hiCON	NoGo errors	High-SPQ	3.714
	130	hiPREP, loCON	NoGo errors	High-SPQ	3.006
	233	hiPREP, loCON	RT	Ave-SPQ	3.247
	217	loPREP, loCON	GoHKRT_Cor	Ave-SPQ	-3.479
	222	loPREP, loCON	GoHKRT_Cor	Ave-SPQ	-3.529
	219	loPREP, hiCON	GoHKRT_Cor	Ave-SPQ	-4.499
	207	hiPREP, hiCON	GoHKRT_Cor	Ave-SPQ	-3.107
	217	loPREP, loCON	HKRT_NoGo_Cor	Ave-SPQ	-3.277
	222	loPREP, loCON	HKRT_NoGo_Cor	Ave-SPQ	-3.273
	219	loPREP, hiCON	HKRT_NoGo_Cor	Ave-SPQ	-4.372
	222	hiPREP, loCON	HKRT_NoGo_Cor	Ave-SPQ	-3.246
	220	loPREP, loCON	Go errors	Ave-SPQ	3.900
	211	loPREP, hiCON	Go errors	Ave-SPQ	3.121
	220	hiPREP, loCON	Go errors	Ave-SPQ	3.250
	211	loPREP, loCON	NoGo errors	Ave-SPQ	3.681
	233	loPREP, hiCON	NoGo errors	Ave-SPQ	3.326

Appendix V Skewed and kurtotic violations in study 2

Violation	Experimental condition	Variable	Group	Z Score
Skewness				
	loPREP, loCON	GoHKRT_Cor	High-SPQ	-4.810****
	loPREP, hiCON	GoHKRT_Cor	High-SPQ	-4.473****
	hiPREP, loCON	GoHKRT_Cor	High-SPQ	-3.134****
	loPREP, loCON	Go errors	High-SPQ	10.035*
	loPREP, hiCON	Go errors	High-SPQ	6.840+
	hiPREP, loCON	Go errors	High-SPQ	4.003*
	loPREP, loCON	NoGo errors	High-SPQ	5.067*
	hiPREP, loCON	NoGo errors	High-SPQ	3.332*
	loPREP, hiCON	GoHKRT_Cor	Ave-SPQ	-3.746****
	loPREP, loCON	NoGo errors	Ave-SPQ	5.457*
Kurtosis	loPREP, loCON	GoHKRT_Cor	High-SPQ	-4.967****
	hiPREP, loCON	NoGoHKRT_Cor	High-SPQ	4.333****
	hiPREP, hiCON	NoGoHKRT_Cor	High-SPQ	8.570****
	loPREP, loCON	Go errors	High-SPQ	24.586+
	loPREP, hiCON	Go errors	High-SPQ	10.205+
	hiPREP, loCON	Go errors	High-SPQ	3.789*
	loPREP, loCON	NoGo errors	High-SPQ	3.740*
	loPREP, hiCON	GoHKRT_Cor	Ave-SPQ	9.543****
	loPREP, hiCON	HKRT_NoGo_Cor	Ave-SPQ	5.188****
	hiPREP, hiCON	HKRT_NoGo_Cor	Ave-SPQ	3.153****
	loPREP, hiCON	HKRT_NoGo-Inc	Ave-SPQ	4.467****
	loPREP, loCON	NoGo errors	Ave-SPQ	6.471*

* squareroot transformation able to normalize distribution
**log transformation able to normalize distribution
***inverse
****cosine
+unsuccessfully transformed

Appendix W. Clinical correlates of AIT#2 experimental variables from study 2

Clinical Measure	Subscale or Factor Score	Experimental Correlate	Experimental Condition	Correlation Coefficient (r)	P Value
SPQ	Cog-Per	loPREP, loCON	NoGo error	r =246	p=.021
	Cog-Per	hiPREP, loCON	NoGo error	r =.286	p=.007
	Cog-Per	hiPREP, hiCON	NoGo error	r =.322	p=.002
	Interpersonal	loPREP, loCON	NoGo error	r =.248	p=.020
	Interpersonal	hiPREP, hiCON	NoGo error	r =.167	p=.012
	IOR	hiPREP, loCON	NoGo error	r =.232	p=.029
	IOR	hiPREP, hiCON	NoGo error	r =.257	p=.016
	ESA	hiPREP, hiCON	NoGo error	r =.228	p=.032
	OB/MT	loPREP, loCON	NoGo error	r =.272	p=.010
	OB/MT	hiPREP, loCON	NoGo error	r =.368	p<.001
	OB/MT	hiPREP, hiCON	NoGo error	r =.241	p=.023
	CA	loPREP, loCON	NoGo error	r =.241	p=.045
	SUS	loPREP, loCON	NoGo error	r =.292	p=.006
	SUS	loPREP, hiCON	NoGo error	r =.211	p=.048
	SUS	hiPREP, loCON	NoGo error	r =.258	p=.015
	SUS	hiPREP, hiCON	NoGo error	r =.406	p<.001
	Cog-Per	loPREP, loCON	Go error	r =.241	p=.023
	Cog-Per	hiPREP, loCON	Go error	r =.220	p=.039
	OB/MT	loPREP, loCON	Go error	r =.263	p=.013
	OB/MT	hiPREP, loCON	Go error	r =.320	p=.002
	Cog-Per	hiPREP, hiCON	GoRT	r =-.295	p=.005
	IOR	hiPREP, hiCON	GoRT	r =-.227	p=.034
	OB/MT	loPREP, loCON	GoRT	r =-.251	p=.018
	OB/MT	hiPREP, loCON	GoRT	r =-.222	p=.038
	OB/MT	hiPREP, hiCON	GoRT	r =-.326	p=.002
	Cog-Per	hiPREP, loPREP	GoHKRT	r =-.225	p=.035
	Cog-Per	hiPREP, hiPREP	GoHKRT	r =-.375	p<.001
	Interpersonal	hiPREP, hiCON	GoHKRT	r =-.329	p=.002
	Disorganized	hiPREP, hiCON	GoHKRT	r =-.259	p=.015
	IOR	hiPREP, hiCON	GoHKRT	r =-.233	p=.029
	ESA	hiPREP, hiCON	GoHKRT	r =-.214	p=.046
	UPE	hiPREP, hiCON	GoHKRT	r =-.229	p=.032
	OEB	hiPREP, hiCON	GoHKRT	r =-.212	p=.047
	NCF	hiPREP, hiCON	GoHKRT	r =-.238	p=.007
	OS	hiPREP, hiCON	GoHKRT	r =-.252	p=.018
	SUS	hiPREP, loCON	GoHKRT	r =-.213	p=.046
	SUS	hiPREP, hiCON	GoHKRT	r =-.395	p<.001
	Interpersonal	hiPREP, hiCON	NoGoHKRT	r =-.215	p=.045
	NCF	hiPREP, hiCON	NoGoHKRT	r =-.221	p=.038
PAI	ANT	hiPREP, hiCON	NoGo error	r =.219	p=.045
	ALC	hiPREP, loCON	Go error	r =.237	p=.030
	ARD	loPREP, loCON	GoRT	r =.232	p=.033

	DEP	loPREP, loCON	GoRT	r =.219	p=.045
NEO-FFI	Agreeableness	loPREP, loCON	NoGo error	r =-.237	p=.026
	A-Trust	loPREP, loCON	NoGo error	r =-.216	p=.043
	A-Straight	loPREP, loCON	NoGo error	r =-.220	p=.039
	E-Activity	hiPREP, loCON	NoGo error	r =.244	p=.022
	O-Values	hiPREP, hiCON	NoGo error	r =-.273	p=.010
	C-Comp	hiPREP, hiCON	NoGo error	r =-.220	p=.039
	C-Dut	loPREP, loCON	NoGo error	r =-.332	p=.002
	C-Dut	hiPREP, hiCON	NoGo error	r =-.279	p=.009
	O-Values	loPREP, hiCON	Go error	r =-.329	p=.002
	A-Straight	hiPREP, hiCON	Go error	r =219	p=.041
	A-Altuism	loPREP, loCON	Go error	r =-.223	p=.036
	C-Dut	hiPREP, loCON	Go error	r =-.218	p=.041
	Extroversion	hiPREP, loCON	GoRT	r =-.227	p=.034
	N-Anxiety	loPREP, loCON	GoRTs	r =.246	p=.021
	E-Activity	hiPREP, hiCON	GoRT	r =-.302	p=.004
	A-Altruism	hiPREP, loCON	GoRT	r =-.217	p=.042
	Conscientiousness	hiPREP, hiCON	GoHKRT	r =.215	p=.044
	E-Activity	hiPREP, loCON	GoHKRT	r =-.242	p=.023
	C-Dut	hiPREP, hiCON	GoHKRT	r =.307	p=.004
	N-Vuln	loPREP, loCON	NoGoHKRT	r =.219	p=.043
WAIS-III	FSIQ_est	loPREP, hiCON	Go error	r =-.279	p=.008
	FSIQ_est	loPREP, loCON	NoGo error	r =-.228	p=.033
	FSIQ_est	hiPREP, hiCON	NoGo error	r =-.219	p=.041

Schizotypal Personality Questionnaire (SPQ):
Factors: COG-PER: Cognitive Perceptual Factor, INT: Interpersonal, DIS: Disorganized
Subscales: IOR: ideas of reference, ESA: excessive Social Anxiety, OB/MG: odd behaviour/magical thinking,
UPE: unusual perceptual experiences, OEB: odd/eccentric behaviour, NCF: no close friends,
OS: odd speech, CA: constricted affect, S: suspiciousness.

PAI subscales:
SOM: Somatic Complaints, ANX: Anxiety, ARD: Anxiety-Related Disorders, DEP: Depression, MAN: Mania,
PAR: Paranoia, SCZ: Schizophrenia, BOR: Borderline, ANT: Antisocial Features, DRG: Drug Problems, ALC:
Alcohol Problems, AGG: Aggression, SUI: Suicidal Ideation, NS: Nonsupport, TR: Treatment Rejection, DOM:
Dominance, WAR: Warmth.

loCON: low CON difficulty
hiCON: high CON difficulty
loPREP: low difficulty PREP condition
hiPREP: high difficulty PREP condition
Go error: error (of omission) on Go Trial
GoRT: Response Time on Go Trials
GoHKRT: HKRT on Go Trial
HKRT: Home Key Release Time
NoGo error: error (of commission) on NoGo Trial
NoGoHKRT: HKRT on NoGo Trial