DUAL-STREAM MODULATION FAILURE, COGNITIVE BIASES AND DELUSIONS IN SCHIZOPHRENIA

by

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A THESIS SUBMITTED IN PARTIAL FULFILLMENT OF
THE REQUIREMENTS FOR THE DEGREE OF

DOCTOR OF PHILOSOPHY

in

THE FACULTY OF GRADUATE STUDIES

(Neuroscience)

THE UNIVERSITY OF BRITISH COLUMBIA
(Vancouver)

April 2012

Abstract

Recent cognitive research has made important contributions to our understanding of delusions, but there have been few attempts to generate a general model that address both delusion formation and maintenance, with a focus on the mechanisms that may underlie the cognitive characteristics of delusions. This thesis describes studies replicating and extending our understanding of two previously identified cognitive biases, and then outlines the development and initial testing of a new model of delusions.

The Dual-Stream Modulation Failure (DSMF) model suggests that delusions are the result of an imbalance between two streams of reasoning: Stream 1, which is automatic and intuitive, and Stream 2, which is slower and more deliberative. The degree to which each stream is favoured in a given situation may depend on two modulators: conflict and emotion. Cognitive conflict may cause an individual to consider the available evidence more carefully, while emotional salience may favour reflexive, non-deliberative processing. In schizophrenia, conflict modulation failure (CMF) and/or accentuated emotional modulation (AEM) may result in an under-recruitment of Stream 2 processing and over-reliance on Stream 1, increasing the likelihood that erroneous interpretations will form and be maintained.

The first study employs a variation of a classic probabilistic reasoning paradigm to provide new insights into to the jumping-to-conclusions and over-adjustment biases. The second study describes the first multivariate analysis of bias against disconfirmatory evidence (BADE) data using all available information from the task to aid interpretation of the cognitive underpinnings of the evidence integration necessary in the BADE task. The third and fourth studies investigate the DSMF model of delusions using a conditional reasoning paradigm that places content believability in conflict with logical validity.

Support is provided for CMF, with the schizophrenia group showing a greater drop in performance and a significantly smaller increase in activity in areas of the brain associated with conflict and deliberative processing for conflict compared to non-conflict stimuli. No evidence was found for AEM, suggesting that future DSMF research may either need to make adjustments to the experimental paradigm or to the model itself.

Preface

With the exception of the introduction and discussion chapters (Chapters One and Seven), all chapters of this thesis have either been published in peer-reviewed journals or are being prepared for submission. A reference list, by chapter, has been provided below.

The journal articles presented in Chapters Two and Three describe collaborative research on cognitive biases in schizophrenia that I conducted with Dr. Todd Woodward, using existing paradigms developed previously by Dr. Woodward's research group. With guidance and editorial input from Dr. Woodward, I analysed and interpreted the data sets, did the background research and wrote the manuscripts. The journal article presented in Chapter Four describes a new model of delusions in schizophrenia, which I developed in collaboration with my supervisor, Dr. Elton Ngan. The study design for Chapters Five and Six were also the result of collaboration between Dr. Ngan and myself. Data collection, data analysis, and manuscript preparation for these papers was carried out by myself, with guidance and editorial input from Dr. Ngan and Dr. Todd Woodward. For Chapter Five, additional input on task design was provided by Dr. Christopher Murray, with Rachel McKay and Manuel Munz providing assistance with data collection and analysis of pilot data.

All research was approved by the UBC Clinical Research Ethics Board (Certificate Number: H07-00044), and the UBC Behavioural Research Ethics Board (Certificate Number: B02-0281).

Chapter Two:

Speechley, W., Moritz, S., Ngan, E., & Woodward, T. (in press). Impaired evidence integration and delusions in schizophrenia. *Journal of Experimental Psychopathology*.

Chapter Three:

Speechley, W., Whitman, J., & Woodward, T. (2010). The contribution of hypersalience to the "jumping to conclusions" bias associated with delusions in schizophrenia. *Journal of Psychiatry and Neuroscience, 35*(1), 7-17.

Chapter Four:

Speechley, W., & Ngan, E (2008). Dual-stream modulation failure: A novel hypothesis for the formation and maintenance of delusions in schizophrenia. *Medical Hypotheses, 70*, 1210–4.

Chapter Five:

Speechley, W., Murray, C., McKay, R., Munz, M., & Ngan, E. (2010). A failure of conflict to modulate dual-stream processing may underlie the formation and maintenance of delusions. *European Psychiatry, 25*(2), 80-6.

Chapter Six:

Speechley, W., Woodward, T., & Ngan, E. (in preparation). The neural correlates of Dual-Stream Modulation Failure in schizophrenia.

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Glossary

AEM	Accentuated emotional modulation
ANOVA	Analysis of variance
ANCOVA	Analysis of covariance
BADE	Bias against disconfirmatory evidence
BOLD	Blood-oxygen-level-dependent
CEN	Central executive network
CMF	Conflict modulation failure
dACC	Dorsal anterior cingulate cortex
df	Degrees of freedom
D/LPFC	Dorsal/lateral prefrontal cortex
DMN	Default mode network
DSM-IV-TR	Diagnostic and statistical manual of mental disorders, 4th Edition, text revision
DSMF	Dual-stream modulation failure
fMRI	Functional magnetic resonance imaging
HC	Healthy control group
JTC	Jumping-to-conclusions
K-BIT	Kaufman brief intelligence test
MCT	Metacognitive training
MINI	The mini-international neuropsychiatric interview
NART	National adult reasoning test
OFC	Orbitofrontal cortex

PCA	Principal component analysis
QUICK	Ammons quick test
SD	Standard deviation
SEM	Standard error of the mean
SSPI	Signs and symptoms of psychotic illness scale
Sz	Schizophrenia group
VMPFC	Ventromedial prefrontal cortex

Acknowledgements

This PhD would not have been possible without the guidance, support and friendship of my supervisor, Dr. Elton Ngan, and Dr. Todd Woodward.

I would also like to thank Dr. Alex MacKay and the members of the MRI Research Centre, Trudy Harris, Paul Hamill, Linda James and Linda Zimmer, for their invaluable assistance with the collection of my fMRI data, and the good conversation across many, many hours of scanning.

I owe much of my development as a researcher to help and advice from good friends in the Schizophrenia, Cognition and Imaging Lab (Sara Weinstein, Andrea Javor, Hossein Faramarzi, Rachel McKay, Navi Dharampal, and Manuel Munz), and the Cognitive Neuroscience of Schizophrenia Lab (Paul Metzak, Jennifer Whitman, and Liang Wang).

Special thanks to my friends and family for supporting me through the good times, the bad times, and the very bad times these last five years; in particular, my immediate family: Keely Speechley, Jacob Speechley, Chrissie Speechley, John Speechley, Lucy Speechley, Paul Keep, Fynley Keep, Linda Carswell-Bland, Richard Bland, and Gordon Hammond.

This thesis was made possible by financial support from the Mind Foundation of British Columbia, the Michael Smith Foundation for Health Research, and the Canadian Institutes of Health Research.

Dedication

For Keely, Jacob, and Peanut.

Chapter One: An introduction to delusions in schizophrenia

1.1 Introduction: Schizophrenia and delusions

Schizophrenia is a chronic, debilitating illness that affects 1% of the world's population (World Health Organization, 1996). Its effects are often devastating to both the individuals affected by the illness and their families. Despite ongoing improvements in pharmacotherapy and services for patients with schizophrenia, the worldwide economic burden of this disorder remains substantial. Medications are only partially effective for some people and completely ineffective for others. Treatment and rehabilitation programs provide support and alleviate suffering to some degree, but only to those with the insight to accept help. We are far from a cure, treatment programs are suboptimal, and the toll of schizophrenia on the individual and their families remains unacceptably high. Further improvements in treatment require more accurate models of the psychological mechanisms that underlie the symptoms of schizophrenia.

Delusions are one of the hallmark symptoms of psychosis. For a diagnosis of schizophrenia using the DSM-IV-TR (American Psychiatric Association, 2000), delusions are considered one of the "two or more" characteristic symptoms that must be present "for much of the time during a one-month period". If a delusion is bizarre, it alone is sufficient for a diagnosis of schizophrenia, provided that it also meets the duration criteria. Modern definitions of delusions continue to bear a striking resemblance to Jasper's (1913) three criteria for judging a belief to be delusional: conviction/certainty, incorrigibility, and impossibility/falsity. For example, the DSM-IV-TR defines delusion as:

"A false belief based on incorrect inference about external reality that is firmly sustained despite what almost everyone else believes and despite what constitutes incontrovertible and obvious proof or evidence to the contrary. The belief is not one ordinarily accepted by other members of the person's culture or subculture (e.g., it is not an article of religious faith)."

A number of different approaches have been employed across the last century in the classification of delusions by content. Kraepelin (1919) considered there to be six major categories of delusions: ideas of sin, ideas of persecution, ideas of influence, exalted ideas, sexual ideas, and ideas of reference. The most detailed, recent classification of delusions by content appears in the Present State Examination (Wing, Cooper & Sartorius, 1974), which identifies 13 themes: persecution, guilt, self-depreciation, nihilistic, grandeur, reference, hypochondriacal, special mission, religious, fantastic, sexual, impending doom, and control. More detailed descriptions of some of these categories of delusion are provided below (adapted from McKenna, 2007):

Persecutory delusions are the belief that an outside force, power, organization or individual has harmed or is attempting to harm the individual in some manner, including physical threat, torment, and slander. These beliefs may be relatively simple in form or maybe incredibly complex and even bizarre.

Grandiose delusions may encompass special powers, abilities, and knowledge or the belief of grandiose identity, which may include the belief that the individual is a specific famous or powerful individual. Religious delusions may also be grandiose in nature, such as beliefs of divine purpose or identity.

Delusions of reference refer to the experience of neutral events taking on self-referential significance, such as the belief that the television or radio is making references to the individual or that the incidental gestures of strangers are deliberate messages to or about the individual.

Somatic/hyperchondriacal delusions are the belief that the body is diseased, rotten or altered in some manner, such as the belief that the body is infested with parasites or contains foreign objects.

1.2 Concern over the definition of delusions

While delusions are one of the cardinal symptoms of schizophrenia, there is ongoing concern over the acceptability of the very definition of delusion, with contention extending to all elements of the DSM definition (Spitzer, 1990; David, 1999). The first problem identified is the suggestion of falsity as a requirement for a diagnosis of delusions. Falsity may be difficult to definitively or practically ascertain for a clinician, and it may not even be a necessary requirement for delusion. The latter situation is exemplified in delusions of jealousy where a patient's belief can be considered unfounded based on the evidence available to them, but where infidelity is, in fact, occurring unbeknownst to the individual. Religious beliefs may also be problematic, particularly where judgments are being made regarding the sufficiency of the evidence for accepting a belief or whether the beliefs are shared by others in an individual's community.

High conviction levels and incorrigibility in the face of contradictory evidence are not peculiar to delusions, with research showing overconfidence in the decisions of healthy individuals (e.g., Fischhoff, Slovic & Lichtenstein, 1977; Fischhoff & Beyth-Marom, 1983). Gazzaniga (1985) even suggests that this may be adaptive, serving to preserve "cognitive consistency". However, authors such as Strauss (1969) indicate that the difference between "normal" reasoning and delusions may be the degree of conviction, not its presence, fitting with suggestions that delusions may lie on a continuum with "normal" beliefs (Kendler, Glazer & Morgenstern, 1983; Spitzer, 1990; Butler & Braff, 1991; Peters, Joseph & Garety, 1999; Appelbaum, Robbins & Roth, 1999).

The definition of delusions has changed little since Jaspers (1913) suggested his three criteria, but research has led to some changes in thinking about delusions that are not reflected in the DSM-IV-TR definition. Rather than being a categorical entity, where delusions are either present or absent, delusions may differ along a number of dimensions that may vary continuously across time and in response to cognitive-behavioural treatments (Strauss, 1969; Kendler, Glazer & Morgenstern, 1983; Garety, 1985; Brett-Jones, Garety & Hemsley, 1987; Garety & Hemsley, 1987; Oltmanns & Maher, 1988; Chadwick & Lowe, 1990; Tarrier et al., 1993; Kuipers et al., 1997; Tarrier et al., 1998; Jakes, Rhodes & Turner, 1999; Sensky et al., 2000). Different factor analysis rotations have suggested that this multidimensionality may encompass either four dimensions (distress, belief, strength, and obtrusiveness/concern; Garety & Hemsley, 1987) or five (conviction, extension, bizarreness, disorganization, and pressure; Kendler, Glazer & Morgenstern, 1983).

Despite genuine concerns regarding the applicability of typical definitions of delusion to all cases of delusions, it remains a concept with widespread clinical acceptance (Bell, Halligan & Ellis, 2006a). This is likely due to fact that the caveats regarding the acceptability of current definitions only become diagnostically significant for delusion cases on the fringes of classification, with the majority of cases being unambiguous, and adequately captured by current definitions of delusions. A review of papers that reported inter-rater reliabilities for delusion diagnosis indicated values ranging from 0.61 to 0.80 for structured clinical interviews, with the strongest inter-rater reliabilities for incidences where standardised scales were used, as is increasingly common in research studies (Bell, Halligan & Ellis, 2006b).

1.3 Theories of delusions

Thematically, Gibbs and David (2003) grouped theories of delusions into three categories: motivational, perceptual and cognitive. This is similar to Winters and Neale's (1983) motivation and defect groupings, where the perceptual and motivational categories are effectively collapsed, with the defect and cognitive categories being somewhat equivalent. The research conducted in this thesis falls under the cognitive/defect category of delusion theories, so greater consideration is given to research informing this approach.

1.3.1 Motivational theories of delusions

Motivational theories tend to be specific to certain forms of delusions, indicating how the salient themes and content associated with specific subsets of delusions are adopted through processes such as attributional biases and the avoidance or reduction of anxiety. For example, in anxiety avoidance theories, delusions protect self-esteem by shielding an individual from the experience of negative emotions (e.g., Dollard & Miller, 1950; Cameron, 1955; Cameron, 1959; Shimkunas, 1972; Colby, 1975). Cameron and Colby's theories incorporate psychoanalytic concepts, such as the projection of mistrust or transference of blame to others as a form of ego-defense (e.g., Freud, 1915), though research with healthy individuals has suggested that projection may not necessarily be associated with a reduction in anxiety (Holmes, 1974).

Maher's (1974) perceptual abnormality account fits with the motivational approaches, despite highlighting altered perceptual experience as a primary factor in the development of delusion. Delusions are seen as the product of an intact reasoning system attempting to make sense of abnormal input, with the level of conviction in the belief being no different from the strongly held beliefs of healthy individuals. By "successfully" generating an account for anomalous experiences, anxiety reduction is achieved, providing reinforcement that may contribute to the maintenance of the delusion. While the perceptual abnormality account seems useful in explaining the content of certain delusions, this account cannot explain delusions that occur in the absence of perceptual aberrations, does not address why more plausible explanations for these experiences are not favoured, and is not consistent with more recent research that has identified reasoning biases in people with delusions.

The "Theory of Mind deficit" (Frith, 1992) and "Attributional Bias" account (Bentall, Kaney & Dewey, 1991; Bentall, Kinderman & Kaney, 1994) are motivational theories that are specific to persecutory delusions and delusions of reference. The attributional bias account suggests that persecutory delusions may function as a self-esteem defense mechanism, serving to minimize differences between the "actual self" and the "ideal self" by holding others responsible for negative events (i.e., externalizing and personalizing) and taking credit for positive events (i.e., internalizing) (Bentall, Kaney & Dewey, 1991; Bentall, Kinderman & Kaney, 1994; Kinderman & Bentall, 1996). Some experimental evidence supports a higher rate of external attributions for negative events

(Sharp et al., 1997), but there is little support for an increased likelihood to take credit for positive events (review: Garety & Freeman, 1999). Other research has indicated that it may be less a case of externalizing or internalizing, but rather personalizing, blaming others for negative events (Kinderman & Bentall, 1997; Beck & Proctor, 2002; Freeman & Garety, 2004).

The theory of mind deficit hinges on the hypothesis that persecutory delusions represent a misinterpretation of the thoughts, beliefs and intentions of other individuals, leading to the misidentification of malevolence where none exists. The support for this bias in people with persecutory delusions has been equivocal (review: Garety & Freeman, 1999), with deficits on theory of mind tasks showing a stronger association with negative symptoms (Doody, Gotz, Johnstone, Frith & Owens, 1998; Mitchley, Barber, Gray, Brooks & Livingstone, 1998). However, this finding may simply reflect the greater general cognitive deficits of patients with negative symptoms (Langdon et al., 1997).

1.3.2 Cognitive theories of delusions

Unlike motivational theories, cognitive approaches have tended not to provide explanations for why certain content is salient to individuals with specific forms of delusions, focusing instead on underlying deficits in reasoning that may be common to multiple categories of delusions.

One paradigm has been particularly fruitful in the generation of cognitive theories of delusions; the probabilistic reasoning paradigm referred to as the “beads task”. In the standard version of the beads task (Huq, Garety & Hemsley 1988), participants are shown two jars of beads containing reverse ratios of two different coloured beads (e.g., one jar with an 85:15 ratio of pink to green beads, and another jar with an 85:15 ratio of green to pink beads). Participants are shown a series of beads, one at a time, and are required to guess from which jar the experimenter is taking beads. Instructions are given to make it clear that the experimenter is drawing beads from only one of the jars, and that the beads are being returned to the jar after each draw to maintain the same bead ratio across the series of draws.

In the delusions literature, the beads task it most closely associated with the "jumping-to-conclusions" (JTC) bias (Huq, Garety & Hemsley 1988; Garety, Hemsley & Wessely, 2001), whereby participants with delusions request significantly fewer bead draws before deciding which jar the experimenter is drawing beads from. This effect does not appear to be associated with impulsivity as changing the ratio of the beads in each jar also changes the amount of evidence people diagnosed with schizophrenia request before making a decision (Dudley, John, Young & Over, 1997). JTC is not considered to be indicative of a probabilistic reasoning or hypothesis testing deficit (Garety & Freeman, 1999), but rather, a bias towards the early acceptance of hypotheses. Thus, the JTC data gathering bias suggests that a more circumscribed approach to data gathering may result in erroneous beliefs being more readily accepted in delusion formation despite minimal evidential support.

One series of experiments has suggested that the JTC effect may be confined to situations where there is lower ambiguity, as in cases of highly contrasting bead colour ratios in a binary choice beads paradigm (Moritz, Woodward and Lambert, 2007). This conclusion was reached after noting the eradication of the JTC effect when the choice was between four jars rather than two. This was predicted by the authors' Liberal Acceptance (LA) account of delusions. Like JTC, LA proposes that limited evidence can elicit resolute decisions under some conditions. It differs from JTC in its introduction of an acceptance threshold beyond which an option must pass before a decision is made. When there are few choice options, as in the standard beads task (Huq, Garety & Hemsley, 1988; Garety, Hemsley & Wessely, 1991), the evidence for one option quickly passes the lowered threshold for acceptance in schizophrenia (Moritz, Woodward and Lambert, 2007). However, when there are multiple response options, the lowered threshold results in more options being accepted as plausible, heightening ambiguity and delaying a definite decision (Moritz, Woodward & Lambert, 2007; Moritz & Woodward, 2004; Moritz, Woodward & Hausmann, 2006). A LA data gathering bias may lead to a greater willingness to give consideration to options that should otherwise be readily discarded as implausible early in the decision-making process, and as such, has been suggested as a factor in the formation of delusions.

The incorrigibility of delusions is well captured by research on the bias against disconfirmatory evidence (BADE). BADE tasks require individuals to rate and re-rate the plausibility of different scenario explanations as incoming information gradually disambiguates the true nature of the event (see Appendix I for examples from the most current BADE paradigm). Some of the scenario explanations are “lure items” that initially appear plausible, but become increasingly implausible with each new piece of disambiguating information. Trials are constructed such that the single “true” explanation initially appears to provide a weak explanation for the event, though gradually becomes the most plausible explanation across a trial. BADE has typically been measured by comparing the degree to which plausibility ratings for lure items are down-rated as incoming evidence indicates their poor explanatory power. People diagnosed with schizophrenia make significantly smaller downward adjustments in plausibility ratings for lure items than healthy controls (Moritz & Woodward, 2006; Woodward, Moritz, Menon & Klinge, 2008).

Data is also available suggesting that the effect is stronger for delusional patients (Woodward, Moritz & Chen, 2006; Woodward, Moritz, Cuttler & Whitman, 2006), and is not associated with IQ measures (Woodward, Buchy, Moritz & Liotti, 2007). There is substantial experimental support for BADE, both in the form of experimental replication and identification of the bias using different versions of the task utilising either pictorial stimuli (Woodward, Moritz, Cuttler & Whitman, 2006; Moritz & Woodward, 2006) or written scenarios (Woodward, Moritz and Chen, 2006; Woodward, Moritz, Menon & Klinge, 2008).

1.3.3 Aberrant salience

The aberrant salience hypothesis of psychosis represents an attempt to bridge neurochemical dysfunction and the symptomatic expression of psychosis, describing how dysregulated dopamine transmission may contribute to the expression of delusional beliefs (Kapur, 2003; Kapur, 2004; Kapur, Mizrahi & Li, 2005). The mesolimbic dopamine system may mediate "attributional salience", with salience attached to thoughts and events owing to their association with rewards or punishments. In delusions, stimulus-independent dopamine release may create, rather than mediate salience, aberrantly attaching salience to neutral thoughts and events. This may contribute to a promdromal state where percepts and ideas take on exaggerated importance, and anxiety is heightened. In this model, delusions are an attempt to explain these aberrantly salient experiences, with the generation of an explanation reducing anxiety and providing a framework in which a bias towards the collection of confirmatory evidence can operate. The specific content of the delusional belief is likely to reflect themes already important to an individual, consistent with their cultural experience. Kapur suggests that differences between individuals may also stem from differences in the interaction of the suggested aberration in dopamine function with factors such as JTC, theory of mind deficits, attributional biases, and perceptual aberrations. There have been few studies testing the aberrant salience hypothesis as of yet, but it stands out as one of the few theories to suggest an underlying mechanism to account for aberrations in cognition that may contribute to delusions.

1.4 Conclusion and research goals

An important contribution of the existing cognitive research to our understanding of delusions has been the identification of general reasoning deficits in schizophrenia that extend beyond the circumscribed domain of the delusions themselves, and can be identified with delusion neutral content couched within non-naturalistic experimental designs. The BADE literature provides an experimental validation of the incorrigibility alluded to in most definitions of delusions, while utilising delusion neutral scenarios. The JTC literature employs a family of abstract, probabilistic reasoning paradigms to explore an information gathering bias that may contribute to the formation of delusions, indicating the tendency of people with delusions to request significantly less evidence before making firm decisions.

While the cognitive literature on delusions has been successful in identifying general cognitive biases that may contribute to delusion formation and maintenance, there have been few attempts to account for why these reasoning biases occur in the first place. Kapur’s aberrant salience hypothesis identifies known differences in dopamine transmission to provide a potential mechanism to account for how ideas can become imbued with aberrant salience in delusions. However, it does not provide a mechanism to account for how heightened salience interacts with reasoning to result in the pathological discounting of overwhelming contradictory evidence in delusion formation and maintenance.

This thesis will attempt to make novel contributions to our understanding of delusion formation and maintenance in schizophrenia by:

1. Conducting studies to replicate and extend our understanding of previously identified cognitive biases (specifically, JTC and BADE)
2. Developing a new model of delusions (Dual-Stream Modulation Failure), which offers mechanisms to account for why there is an insensitivity to disconfirmatory evidence in delusions and how aberrantly accentuated salience may facilitate the acceptance and maintenance of erroneous beliefs
3. Conducting preliminary research to test and refine the Dual-Stream Modulation Failure model

Chapter Two: Reconsidering the "Jumping-to-Conclusions" bias associated with delusions in schizophrenia[1]

2.1 Introduction

An influential and well-supported cognitive bias in the schizophrenia literature is the "jumping-to-conclusions" (JTC) bias (Huq, Garety & Hemsley, 1988; Garety, Hemsley & Wessely, 1991). It describes a reasoning style in patients with delusions that is characterized by early, resolute decisions made on the basis of little evidence. This reasoning bias has been frequently identified by use of the beads task. Typically, two jars of beads are presented to participants, one containing substantially more pink than green beads and the other containing the reverse (Huq, Garety & Hemsley, 1988). One by one, beads are taken from a single hidden jar and presented to the participants who are required to guess from which jar the experimenter is taking beads. In some JTC tasks, the dependent measure is the number of beads drawn before the participant indicates readiness to decide on a jar (draws to decision). Other tasks involve a rating comparing the jars after each bead is drawn (graded estimates). Participants with delusions tend to make firm decisions as to the identity of the jar much sooner than controls, occasionally after the very first bead is presented. In addition to the JTC bias, the beads literature has also reported what has been referred to as either an "over-adjustment bias" (Moritz & Woodward, 2005; Langdon, Ward & Coltheart, 2010) or a "bias towards disconfirmatory evidence" (Garety, Hemsley & Wessely, 1991) in people with delusions. This effect has been suggested due to evidence

[1] A version of this chapter has been published. Speechley, W. J., Whitman, J. C., & Woodward, T. S. (2010). The contribution of hypersalience to the "jumping to conclusions" bias associated with delusions in schizophrenia. *Journal of Psychiatry & Neuroscience, 35*(1), 7-17.

of downward over-adjustments in probability estimates following a single instance of disconfirmatory evidence.

Delusions research involving the beads task has its roots in Hemsley and Garety's theoretical examination of the Bayesian formula as a tool for characterizing the reasoning of patients with delusions (Hemsley & Garety, 1986). This hypothesis paper was followed by Huq, Garety and Hemsley's seminal paper using the beads task with delusional patients (1988). In addition to noting the tendency of delusional patients to make firm decisions on the basis of relatively little evidence, this research suggested that the apparently hasty decision-making style of deluded participants was actually closer to rationality, according to Bayes' theorem, with controls appearing overly cautious in their assessments of probabilities on the beads task.

While the Bayesian model presents the mathematically optimal strategy for probabilistic inferences, it is not expected that any group will follow this pattern of responding because, irrespective of mental health status, people do not necessarily reason logically (Tversky & Kahneman, 1974; Tversky & Kahneman, 1983; Evans, 1989; Garety & Freeman, 1999). Indeed, reasoning in a more Bayesian manner may not even be the most ecologically valid strategy, such that the apparently "more Bayesian" earlier decisions of people with delusions may predispose this group towards making more erroneous decisions under certain everyday circumstances. In this regard, the relative conservatism of controls may contribute to resistance to delusion formation in real-world settings. Nevertheless, normative frameworks, such as Bayes' theorem, provide a useful gauge against which the reasoning of different groups can be compared (Fischhoff & Beyth-Marom, 1983). The Bayesian model of probabilistic reasoning is a particularly suitable framework given the incorporation of prior beliefs and the relative influence of new information on these beliefs.

Despite the consideration given by Hemsley and Garety (1986) to how reasoning biases in delusions could occur given deviations from the Bayesian model at one or more of the formula's various stages, explicit manipulation of or attention to elements of the Bayesian formula in the beads and JTC literature has been largely neglected. In the current study, we considered individual components of the Bayesian formula to develop a more precise understanding of the nature of the JTC reasoning bias in schizophrenia patients with delusions.

Previous studies of JTC have either not compared delusional to non-delusional patients or have included too few participants with schizophrenia to investigate the impact of severe delusions. In this study, we attempted to recruit a large enough sample of participants with schizophrenia to set relatively high cut-offs for delusion severity for inclusion in the delusions group. In addition, we collected data about a group of people diagnosed with bipolar disorder as a psychiatric control group, to provide a way to check whether performance differences between people diagnosed with schizophrenia and healthy controls extend to a different diagnostic category of mental illness.

We used manipulations based on the Bayesian formula with a variant of the beads task, designed to decrease the abstract nature of the task, to compare deviations from Bayesian reasoning between healthy controls, people with bipolar disorder and people with schizophrenia (Woodward et al., 2009). Instead of two jars containing different proportions of two different coloured beads, our task involved two lakes containing different coloured fish, with a fisherman sequentially presenting catches from one of the two lakes. Previous beads-task research has used a single rating scale with jar A at one end of the scale and jar B at the other. This approach artificially forces estimates of the probabilities associated with each choice to be reciprocal, and, although optimally they should be, participants may not actually rate the choices this way. This imposed reciprocity results in a loss of information and provides poorer estimates of the ratings for each option when comparing responses to those anticipated by the Bayesian formula as it is impossible to know whether a movement in one direction represents a downward rating adjustment for one option, an upward rating for the other, or both. For these reasons, we used a separate rating scale for each lake, allowing independence of probability estimates and no loss of information due to imposed reciprocity.

We expected to observe evidence for a JTC-type bias in the delusions group in the form of much higher ratings after viewing the initial fish than for the other groups. We also anticipated that the delusions group would peak sooner in their ratings of the more likely lake, and/or would continue to give higher ratings than the other groups for the duration of each session.

2.2 Methods

2.2.1 Participants

All participants who took part in the study gave written informed consent after a full explanation of the study and the procedures involved. All experimental procedures were approved by the University of British Columbia Clinical Research Ethics Board.

We recruited 37 people diagnosed with schizophrenia and 41 people diagnosed with bipolar disorder from psychiatric hospitals and community health agencies in and around greater Vancouver, British Columbia. All diagnoses were based on DSM-IV-TR criteria (American Psychiatric Association, 2000) and were taken from a chart review. These diagnoses were based on a multidisciplinary team conference during the first month of admission when the diagnosis is reviewed using all sources of information. If a diagnosis had not been finalized at the time of recruitment, the Mini-International Neuropsychiatric Interview (MINI; Sheehan et al., 1998) was administered on the date of testing to provide a final diagnosis.

Psychopathology was assessed using the Signs and Symptoms of Psychotic Illness scale (SSPI; Liddle et al., 2002), a method of gauging symptom severity using 20 symptom items scored 0–4. The SSPI has a separate item for delusions, with subscales for specific delusion types, making it a particularly suitable tool for the current study. Another advantage of the SSPI is that disorganized and impoverished mental activity are better separated (Liddle et al., 2002; Woodward et al., 2003). The SSPI delusion item was used to divide the schizophrenia group into a severely delusional subgroup (n = 7, delusions item = 4) and a mildly or non-delusional subgroup (n = 30, delusions item < 4). For simplicity, the two groups are referred to in this study as the delusional group and the non-delusional group.

The bipolar disorder group recruited for this study experienced low levels of delusions (no bipolar participants had SSPI delusions scores greater than 2). Participants were excluded if they had ever suffered a head injury or a concussion resulting in a loss of consciousness for 10 minutes or more. Substance abuse was assessed by chart review and interview, and we excluded participants if they met the DSM-IV-TR criteria for an Axis I diagnosis of a substance related disorder (e.g., polysubstance dependence). With the exception of four individuals, the condition of all participants with schizophrenia was stabilized with antipsychotic medications, with most taking atypical antipsychotics. Of the patients in the bipolar group, 11 of 41 were taking atypical antipsychotics, two were taking typical antipsychotics and the remainder were not taking any antipsychotic medication.

Chlorpromazine equivalent values are listed in Table 2.1 (Bezchlibnyk-Butler & Jeffries, 2004).

We recruited 40 healthy controls through advertisement and word-of-mouth. Screening with a medical questionnaire ensured that none of the healthy participants had any current or prior history of psychiatric illness. Additional exclusion criteria were the same as those used for the patient groups.

We excluded participants based on their performance on a control series with uniform fish catches (either all black or all white fish) and 50% black and 50% white fish in both lakes. Participants whose ratings for Lake A and Lake B for the final catch (the tenth fish) did not fall within the 4-point range spanning 3 and 7 (on a scale of 0–10) were excluded from the analysis because we considered this to indicate either a lack of understanding of the task or a failure to adequately attend to the task requirements. We excluded two delusional patients with schizophrenia, five non-delusional patients with schizophrenia, four bipolar controls and five healthy controls because of evidence of not understanding or not engaging with the task. Of the five participants retained in the delusional patient group, one showed severe grandiose delusions and four showed severe paranoid delusions.

All participants were fluent in English. Intelligence estimates were made using the Kaufman Brief Intelligence Test (K-BIT; Kaufman & Kaufman, 1990) for verbal and nonverbal intelligence and the Ammons Quick Test (QUICK; Ammons & Ammons, 1962) for an assessment of current IQ. Socio-economic status was estimated using the Hollingshead Two-Factor Index of Social Position (Hollingshead, 1957) using highest parental occupation and education level.

Table 2.1 Sociodemographic and psychopathological characteristics. Mean values are accompanied by standard deviations (in brackets). Symptom scores are derived from the Signs and Symptoms of Psychotic Illness rating scale.

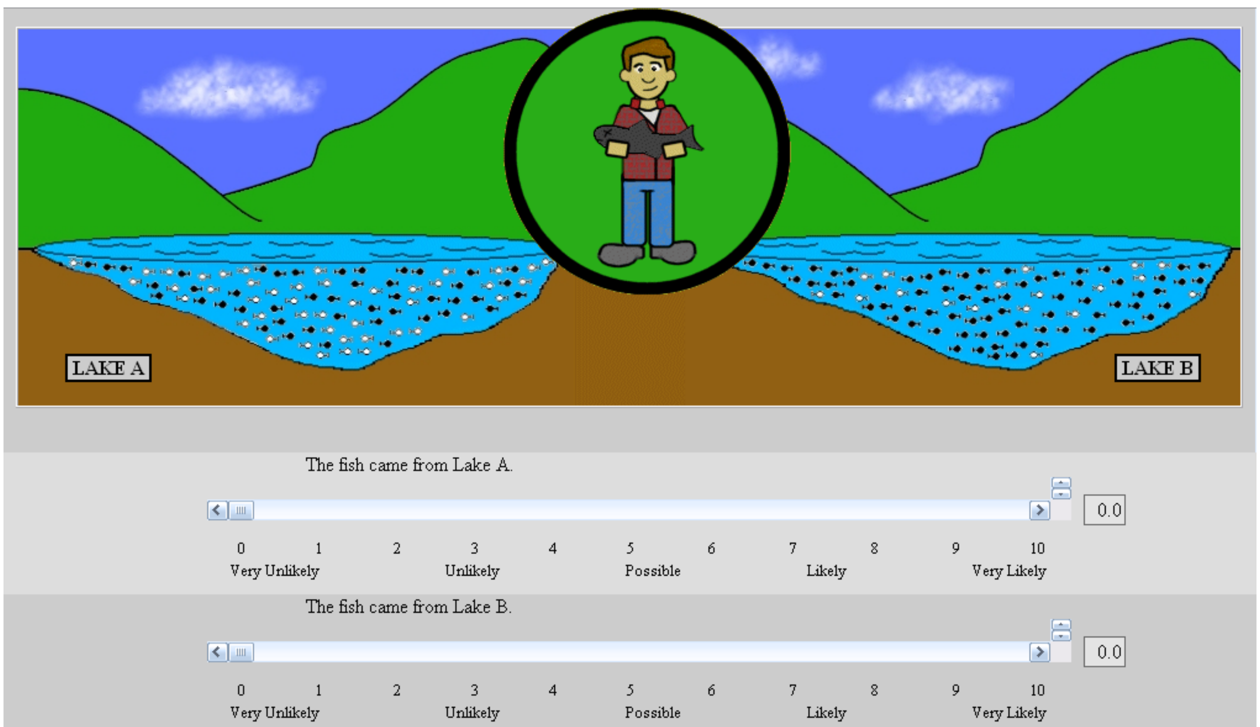
	Healthy (n = 35)	Bipolar (n = 37)	Non-delusional Schizophrenia (n = 25)	Delusional Schizophrenia (n = 5)
Age	35.1 (10.0)*	40.9 (9.5)	37.3 (11.6)	31.2 (10.0)
Age range	19-55	20-56	21-56	18-43
Sex (M:F)	16:19	24:13§	17:8	4:1
Years of education	15.4 (2.4)*‡	15.3 (4.0)†§§	13.0 (3.1)	11.6 (1.7)
QUICK	107.3 (12.1)	112.2 (11.1)§§	102.2(11.6)	101.6 (7.3)
K-BIT vocabulary	107.0 (17.3)*‡	109.4 (18.7)†§§	96.4 (10.6)	90.4 (12.5)
K-BIT matrices	105.8 (18.2)‡	99.8 (9.8)	96.4 (12.5)	98.6 (15.8)
K-BIT composite	107.0 (16.2)	103.7 (9.9)	100.2 (20.8)	94.0 (15.8)
Social status	36.0 (13.7)	30.4 (15.5)	27.2 (14.0)	46.0 (18.4)
Illness duration (years)	n/a	14.2 (9.6)	14.8 (10.9)	13.4 (7.1)
Chlorpromazine Equivalent (mg)	n/a	28.1 (90.2)§	204.7 (401.3)	114.5 (121.9)
Delusions	n/a	0.4 (0.7)††§§	1.2 (1.1)##	4 (0)
- Guilt/Worthlessness	n/a	0 (0.2)	0.1 (0.3)	0 (0)
- Grandiose	n/a	0 (0)††§§	0.3 (0.5)##	1.6 (1.8)
- Paranoid	n/a	0.3 (0.6)††	0.5 (1.1)##	3.8 (0.4)
- Schneiderian	n/a	0.2 (0.5)††	0.4 (0.9)#	1.4 (1.3)
Hallucinations	n/a	0.3 (0.8)†	0.5 (1.2)	1.4 (1.9)
Thought Disorder	n/a	0.2 (0.5)†§	0.8 (1.0)	1.0 (1.4)
Flat Affect	n/a	0.7 (1.0)	0.7 (1.0)	0.2 (0.4)
Poverty of Speech	n/a	0.4 (0.9)	0.3 (0.9)	0 (0)
Underactivity	n/a	1.0 (1.1)	0.7 (0.9)	0 (0)

*Delusional schizophrenia vs. healthy, $p < 0.05$; †Delusional schizophrenia vs. bipolar, $p < 0.05$; ††Delusional schizophrenia vs. bipolar, $p < 0.01$; #Delusional schizophrenia vs. non-delusional schizophrenia, $p < 0.05$; ##Delusional schizophrenia vs. non-delusional schizophrenia, $p < 0.01$; ‡Non-delusional schizophrenia vs. healthy, $p < 0.05$; §Non-delusional schizophrenia vs. bipolar, $p < 0.05$; §§Non-delusional schizophrenia vs. bipolar, $p < 0.01$

2.2.2 The model

We used a computerized task in which, instead of jars of beads, participants saw two lakes containing black and white fish in different ratios. Participants were told that they would see a series of fish caught from only one of the two lakes, with each fish replaced after each catch so as not to alter the ratio of black to white fish in the lake. After each fish in the sequence, participants were instructed to rate on two separate scales the likelihood that the fish were being caught exclusively from Lake A and the likelihood that they were being caught exclusively from Lake B (Figure 2.1; for further examples see Appendix II). The initial prior odds in the Bayesian formula were altered by varying the ratio of one colour fish to the other in each lake across series. Previous research has shown that people with delusions vary their responses in line with changes in the prior odds, indicating that JTC cannot be accounted for by impulsivity (Dudley et al., 1997).

Figure 2.1 Sample screen shot of fishing task. Differences in ratios of black to white fish in each lake for each series were represented graphically. The fisherman was updated for each catch to display the colour of the current fish catch. Following each catch, participants were instructed to make separate ratings of the likelihood that the fish were being caught exclusively from Lake A and the likelihood that they were being caught exclusively from Lake B, using the two sliding scales shown.



We also manipulated the incoming data by presenting mixed and uniform fish series. Mixed series showed fish catches of both colours across a series of catches, whereas uniform series showed fish catches of only one colour. The uniform condition is a useful addition to the more typical mixed series approach, because it reduces any interference arising from cognitive differences in the integration of disconfirming and confirming evidence across a series.

In Bayesian terms, the task can be considered as follows. On viewing the first fish, the initial proportions are the proportion of fish in each lake that match the colour of the viewed fish. On viewing the second fish, the proportions corresponding to the first fish are multiplied by the proportions corresponding to the second fish, which are again simply the proportions of fish of that colour in each lake. The ideal Bayesian reasoner would accurately (1) compute the proportions of fish in each lake that match the colour of the viewed fish, (2) multiply these proportions by those arrived at following the most recent catch and (3) translate those multiplications into a ratio or estimated probability comparing the likelihoods of the two lakes.

The following numerical example is provided to illustrate the influence of our incoming data manipulation. These computations are derived from Bayes' theorem, which can be viewed elsewhere (Bayes, 1763; Laplace, 1814; Hemsley & Garety, 1986). The simplified formulas used were:

$$p(A \sim B) = \frac{p(A)}{p(A) + p(B)} \text{ and } p(B \sim A) = \frac{p(B)}{p(A) + p(B)}$$

where *A* refers to Lake A, *B* refers to Lake B, and *p(A)* and *p(B)* refer to the probability of that the entire current series of fish is being caught independently from Lake A and Lake B, respectively. In the following example, the proportions of fish in each lake are as follows: Lake A contains 80% black fish and 20% white fish, and Lake B contains 30% black fish and 70% white fish. The probability of each lake (and not the other) being correct, after seeing the first fish (black for this example), is computed in four steps:

1. Determine the probability of a black fish being caught from Lake A: 0.8, *p(A)*.
2. Determine the probability of a black fish being caught from Lake B: 0.3, *p(B)*.
3. Compute the probability that the black fish came from Lake A and not Lake B (*p(A~B))* by dividing 0.8 (*p(A)*) by the total of 0.8 + 0.3 (*p(A) + p(B))*, which is 0.8/1.1 = 0.73.
4. Compute the probability that the black fish came from Lake B and not Lake A by dividing 0.3 by the total of 0.8 + 0.3, which is 0.3/1.1 = 0.27.

This means that with 80% black fish and 20% white fish in Lake A and 30% black fish and 70% white fish in Lake B, after viewing the first fish and seeing that it is black, the ideal Bayesian reasoner would compute the probability that the fisherman is fishing from Lake A and not B as 0.73 and the probability that he is fishing from Lake B and not A as 0.27. After viewing a second fish, also black, the probabilities must be adjusted to account for the entire series of fish, as follows:

1. Determine the probability of a second black fish being caught from Lake A: 0.8 × 0.8 = 0.64.
2. Determine the probability of a second black fish being caught from Lake B: 0.3 × 0.3 = 0.09.

3. Compute the probability that the black fish came from Lake A and not Lake B by dividing 0.64 by the total of 0.64 + 0.09, which is 0.64/0.73 = 0.88.
4. Compute the probability that the black fish came from Lake B and not Lake A by dividing 0.09 by the total of 0.64 + 0.09, which is 0.09/0.73 = 0.12.

This means that with 80% black fish and 20% white fish in Lake A and 30% black fish and 70% white fish in lake B, after viewing the first two fish and seeing that they are both black, the ideal Bayesian reasoner would compute the probability that the fisherman is fishing from Lake A and not Lake B as 0.88 and the probability that he is fishing from Lake B and not Lake A as 0.12. Any sequence of fish colours and lake proportions can be incorporated using these four steps. Viewing a third black fish would lead to the following computations:

1. $0.64 \times 0.8 = 0.512$
2. $0.09 \times 0.3 = 0.027$
3. $0.512/(0.512 + 0.027) = 0.95$
4. $0.027/(0.512 + 0.027) = 0.05$

In contrast, viewing a third fish and seeing that it was white would lead to the following computations:

1. $0.64 \times 0.2 = 0.128$
2. $0.09 \times 0.7 = 0.063$
3. $0.128/(0.128 + 0.063) = 0.67$
4. $0.063/(0.128 + 0.063) = 0.33$

In addition to the experimental manipulations carried out with respect to the sequence of the fish catches, the proportion of black to white fish in each lake, and the use of independent rating scales for the two lakes, further changes to the paradigm were made to improve the accuracy of our results compared with previous JTC research. We introduced a control condition to assist in our ability to screen out participants who either did not fully understand the task or were not paying full attention. This condition took the form of a series of catches in which the percentages of fish in the two lakes were 50% black and 50% white, with uniform fish catches. Individuals who showed large deviations in responses from the anticipated estimated probability of 0.5 (50/[50 + 50]) by the end of the series of catches were excluded from further analysis.

2.2.3 Procedure

A computerized beads task variant, using estimates made on a graded response scale (Young & Bentall, 1997), was presented offline using Microsoft Internet Explorer 6.0. This task was written in JavaScript/html, with graphics prepared in Adobe Photoshop CS3. Instead of beads and containers, participants were presented with fish and lakes (Figure 2.1). An image of a fisherman stood between two lakes, with each lake containing a different ratio of black fish to white fish. The lake on the left was designated “Lake A” and the lake on the right, “Lake B.” Each trial consisted of a series of 10 fish being caught, with ratings made after each fish. Participants were told that the fisherman was fishing from only one of the two visible lakes and that he was returning the fish to the same lake after each catch, such that the total ratio of black to white fish did not change across the series. The ratios of black to white fish in each lake were not stated by the experimenter, but they were graphically represented on the screen, to be estimated by the participants.

Each series began with the fisherman holding his current catch (a black or white fish). Participants were instructed to rate how likely they thought it was that he was fishing from Lake A and how likely it was that he was fishing from Lake B following each fish catch in a series. Ratings were made using sliders on two horizontal probability scales, one for each lake, ranging from 0 to 10 (labels were placed below the sliders as follows: 0 = very unlikely, 2.5 = unlikely, 5 = possible, 7.5 = likely, 10 = very likely). The ratings for each lake were independent of each other, such that high ratings for Lake A did not preclude the possibility of giving high ratings for Lake B. A brief practice session was used to familiarize participants with the two sliding rating scales before the experiment began.

The experiment consisted of six series, each comprising 10 fish catches. The ratios of black to white fish in each lake were different for each session (Table 2.2). For series 2, 3, 4 and 6, all 10 fish caught were the same colour. Fish colour varied across series 1 and 5 in the following order (B = black; W = white):

- Series 1: B-W-B-W-W-B-W-B-B-W
- Series 5: B-W-B-B-B-B-W-B-B-B

Lake positions and fish colour for both catches and lake ratios were counterbalanced across series and participants.

Table 2.2 The ratio of the percentage of black to white fish in Lake A and Lake B, and sequence of fish catch colours for Series 1 to 6. Lake positions and fish colour for both catches and lake ratios were counterbalanced across series and participants. Counterbalancing was taken into account by transforming the data such that black fish represented the constant fish colour for series 2, 3, 4 and 6, and the predominant colour in Series 5. For Series 1, where an equal number of black and white fish were caught, the data were transformed such that the first fish caught was set to black. Additionally, lakes were organized such that the lake with the higher proportion of black fish was designated 'Lake A', and the other 'Lake B'.

Series (Catch)	Lake A (B:W)	Lake B (B:W)
1 (B-W-B-W-W-B-W-B-B-W)	50:50	20:80
2 (B-B-B-B-B-B-B-B-B-B)	80:20	20:80
3 (B-B-B-B-B-B-B-B-B-B)	80:20	50:50
4 (B-B-B-B-B-B-B-B-B-B)	50:50	20:80
5 (B-W-B-B-B-B-W-B-B-B)	80:20	50:50
6 (B-B-B-B-B-B-B-B-B-B)	50:50	50:50

Note: B = black fish; W = white fish

2.2.4 Data analysis

The main analyses were carried out separately for uniform and mixed fish series and separately for the ratings of the single lake of the pair that most closely matched the fish colour presented on a given trial, and for the non-matching lake (i.e., the other lake). For example, for Series 2 (Table 2.2) Lake A had a black to white fish ratio of 80:20, while Lake B had a black to white fish ratio of 20:80. All fish caught across Series 2 were black, so Lake A was considered the "matching lake" and Lake B the "non-matching lake", as Lake A had the higher ratio of black to white fish.

These analyses were carried out by way of two 3-way analyses of variance (ANOVAs), with lake ratings as the dependent variable. For the uniform fish series, the ANOVA was based on a 10 × 3 × 4 mixed-model ANOVA, with catches (1–10) and series (2, 3 and 4) as the within-subjects factors and group (delusional schizophrenia, non-delusional schizophrenia, bipolar, and healthy controls) as the between-subjects factor. For the mixed fish series, the ANOVA was a 10 × 2 × 4 mixed model, with catches (1–10) and series (1 and 5) as the within-subjects factors and group (delusional schizophrenia, non-delusional schizophrenia, bipolar, and healthy controls) as the between-subjects factor. Series 6 was not analyzed because it was included in the study as a control condition used to identify and exclude participants who did not understand the task instructions or failed to attend to the task requirements.

2.3 Results

2.3.1 Sociodemographic and psychopathological characteristics

Univariate ANOVAs comparing groups on demographic and IQ measures indicated significant differences between the groups for years of education ($F_{3,85} = 4.52$, $p < 0.01$) K-

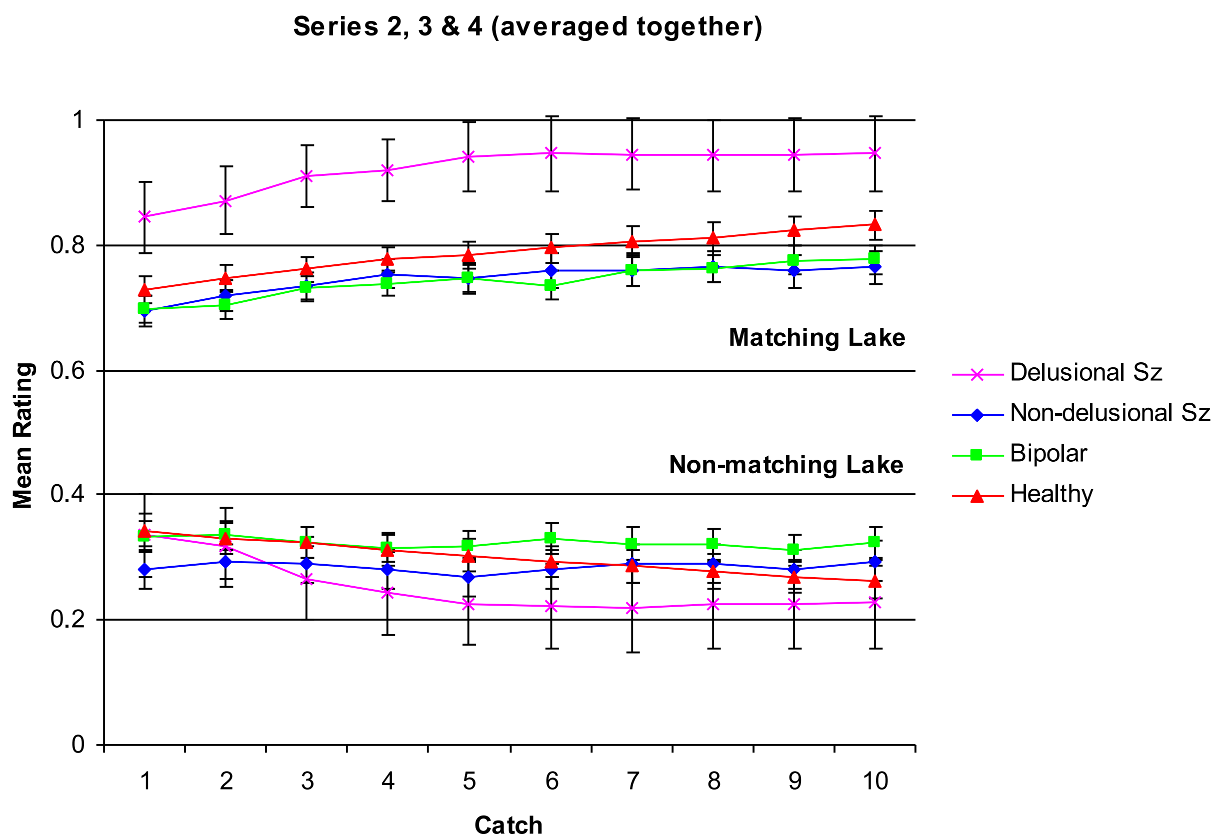
BIT Vocabulary ($F_{3,76} = 4.24$, $p < 0.01$), and QUICK ($F_{3,85} = 4.13$, $p = 0.01$). Sex also differed between groups ($\chi2 = 8.53$, df = 3, $n = 102$, $p < 0.05$). The socio-demographic characteristics of the sample are summarized in Table 2.1. There was no significant difference between the delusional and non-delusional schizophrenia groups for any variable, with the exception of delusion-related symptom scores.

2.3.2 Uniform coloured fish series

For the matching lake ratings (i.e., ratings for the lake which provided the best match to the series of fish catches), there were significant main effects of catches ($F_{9,882} = 11.65$, $p < 0.001$) and series ($F_{2,196} = 14.13$, $p < 0.001$), but these factors did not interact, ($F_{18,1764} = 0.22$, $p = 1.00$). The catches effect was characterized by a strong linear increase over the 10 draws ($F_{1,98} = 15.29$, $p < 0.001$) combined with quadratic and cubic trends ($F_{1,98} = 8.75$, $p < 0.005$; $F_{1,98} = 4.36$, $p < 0.05$), such that the slope of the linear increase flattened with later draws, with no other trends being significant (all *ps* > 0.46). The series effect was characterized by different average ratings for the matching lake over series 2, 3 and 4 (means of 0.85, 0.81, and 0.74, respectively). Although all three series had an 80:20 matching fish ratio, higher ratings for Series 2 were expected because the competing lake had a 20:80 ratio as opposed to a 50:50 ratio for series 3 and 4 (Table 2.2).

The effects of catches and series did not interact with group (all *ps* > 0.76); therefore, we averaged the group comparisons over catches and series. The group effect was highly significant ($F_{3,98} = 4.60$, $p < 0.005$). As can be seen in Figure 2.2 (averaged over series 2–4), this effect was characterized by the rating of the matching lake being significantly higher for the delusional schizophrenia group (mean 0.92) compared to the averaged ratings of the non-delusional schizophrenia group (mean 0.75), bipolar group (mean 0.74), and healthy control group (mean 0.79) ($F_{1,98} = 10.44$, $p < 0.005$).

Figure 2.2 Average matching lake (above) and non-matching lake (below) ratings for Series 2, 3 and 4. A “match” is a situation where the ratio of fish in one lake makes it the best choice with regards to the colour of the current fish catch. Error bars represent the standard error of the mean.

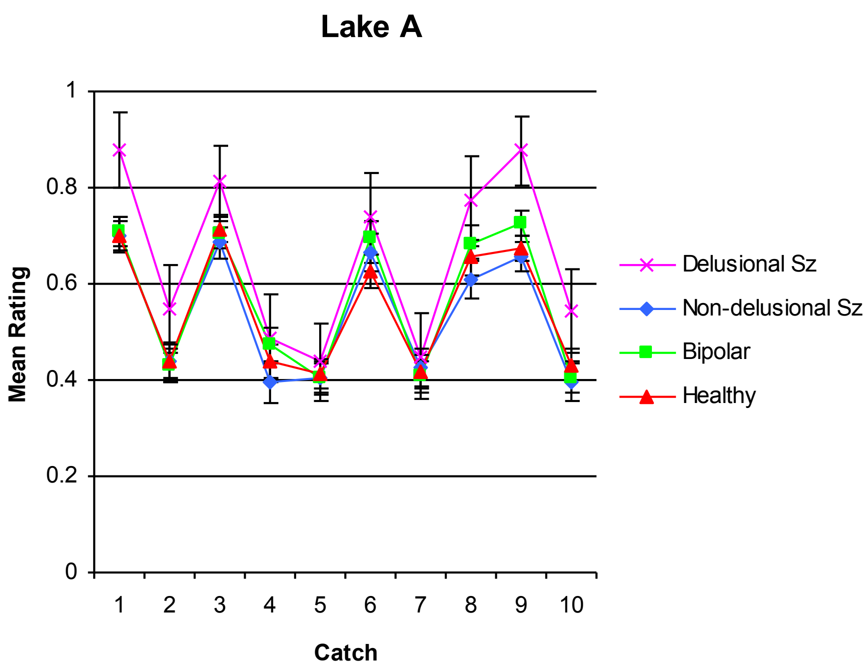


For the non-matching lake ratings, there were significant main effects of catches ($F_{9,882} = 4.14$, $p < 0.001$) and series ($F_{2,196} = 10.45$, $p < 0.001$), but these factors did not interact ($F_{18,1764} = 0.62$, $p = 0.88$). The catches effect was characterized by a linear decrease over the 10 draws ($F_{1,98} = 5.00$, $p < 0.05$), combined with a quadratic trend ($F_{1,98} = 6.91$, $p < 0.01$) such that the slope of the linear decrease flattened with later draws, with no other trends being significant (all *ps* > 0.11). The series effect was characterized by different average ratings for the matching lake over the series, with Series 2 (mean 0.24) having lower ratings than either series 3 or 4 (means of 0.29, and 0.34, respectively). Lower ratings for Series 2 were expected because the non-matching lake had a 20:80 ratio as opposed to 50:50 for series 3 and 4 (Table 2.2). The effects of catches and series did not interact with group (all *ps* > 0.15). Therefore, we averaged the group comparison over catches and series. Unlike the matching lake, the group effect was not significant for the non-matching lake ($F_{3,98} = 0.63$, $p = 0.58$).

2.3.3 Mixed-colour fish series

The progression of ratings for series 1 and 5 (Figure 2.3 and Figure 2.4, respectively) suggests that the delusional schizophrenia group rated the plausibility of the lake that best matched the presented fish higher than did the other groups in any given trial. There were no group differences for ratings of the lake that did not match the presented fish in any given trial.

Figure 2.3 Ratings for Series 1 (Lake A and B) plotted as a function of catches. Counterbalancing was accounted for by designating Lake A as the lake best supported by the first fish catch. Error bars represent the standard error of the mean.



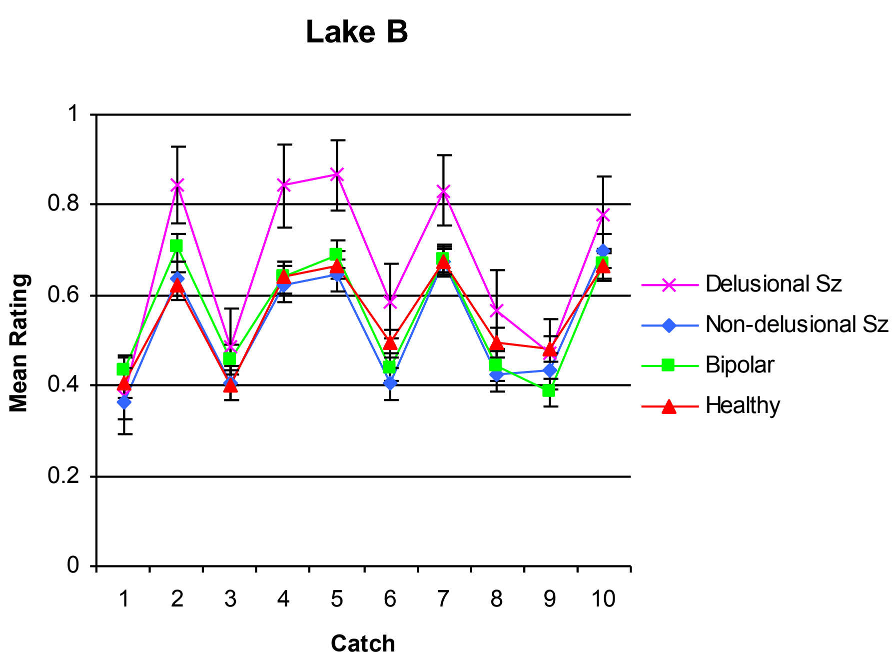
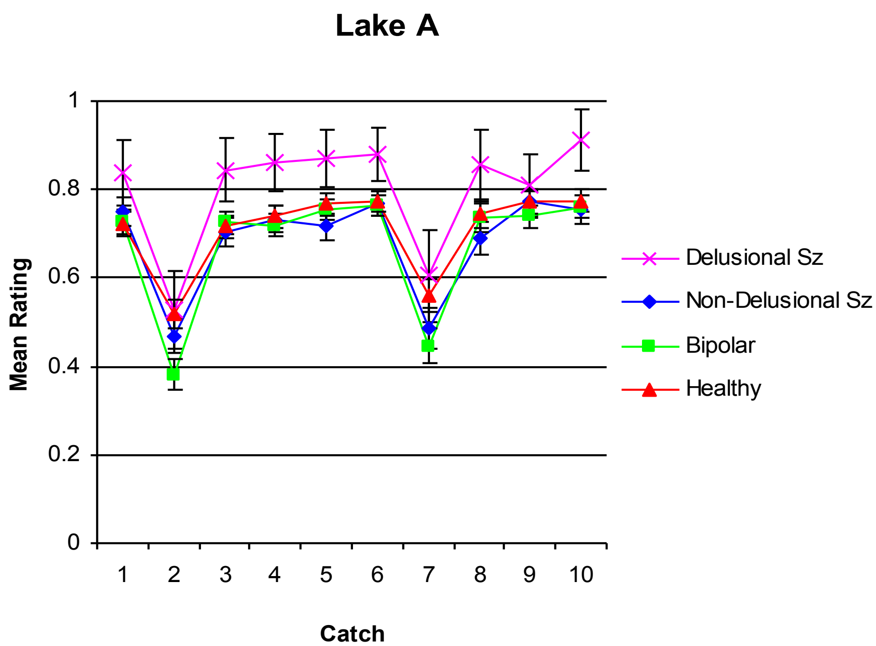
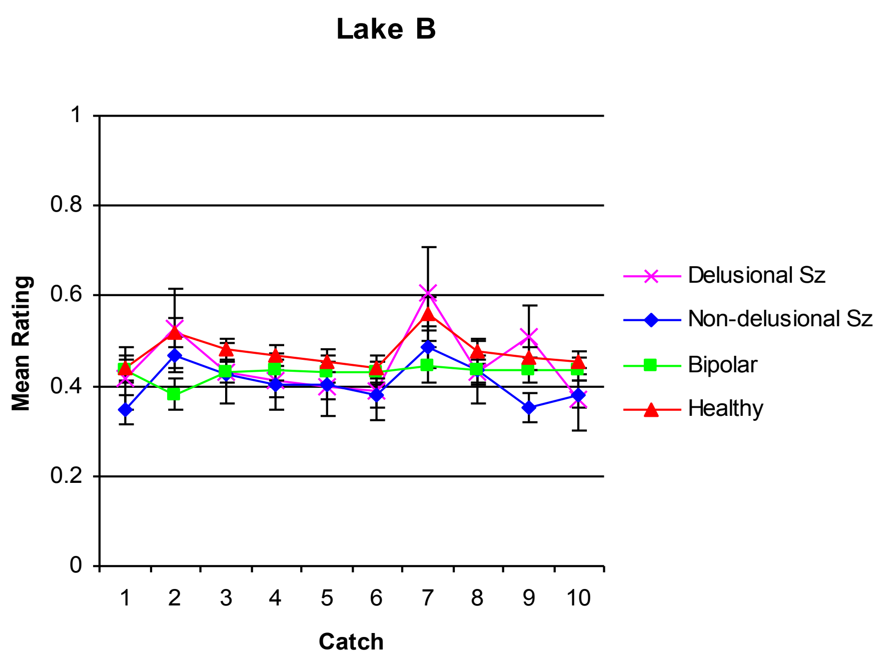


Figure 2.4 Ratings for Series 5 (Lake A and B) plotted as a function of catches. Counterbalancing was accounted for by designating Lake A as the lake best supported by the majority of the fish catches. Error bars represent the standard error of the mean.





For the matching lake ratings, there was a significant main effect of catches ($F_{9,882}$ = 5.97, $p < 0.001$), and this interacted significantly with series ($F_{9,882} = 14.13$, $p < 0.001$). The source of this interaction was that there was no significant effect of catches for Series 1 ($F_{9,882} = 1.33$, $p = 0.22$) but there was for Series 5 ($F_{9,882} = 15.29$, $p < 0.001$). For Series 5, the linear effect was significant ($F_{1,98} = 6.03$, $p < 0.05$), reflecting increasing ratings over the 10 catches. This was not the case for Series 1.

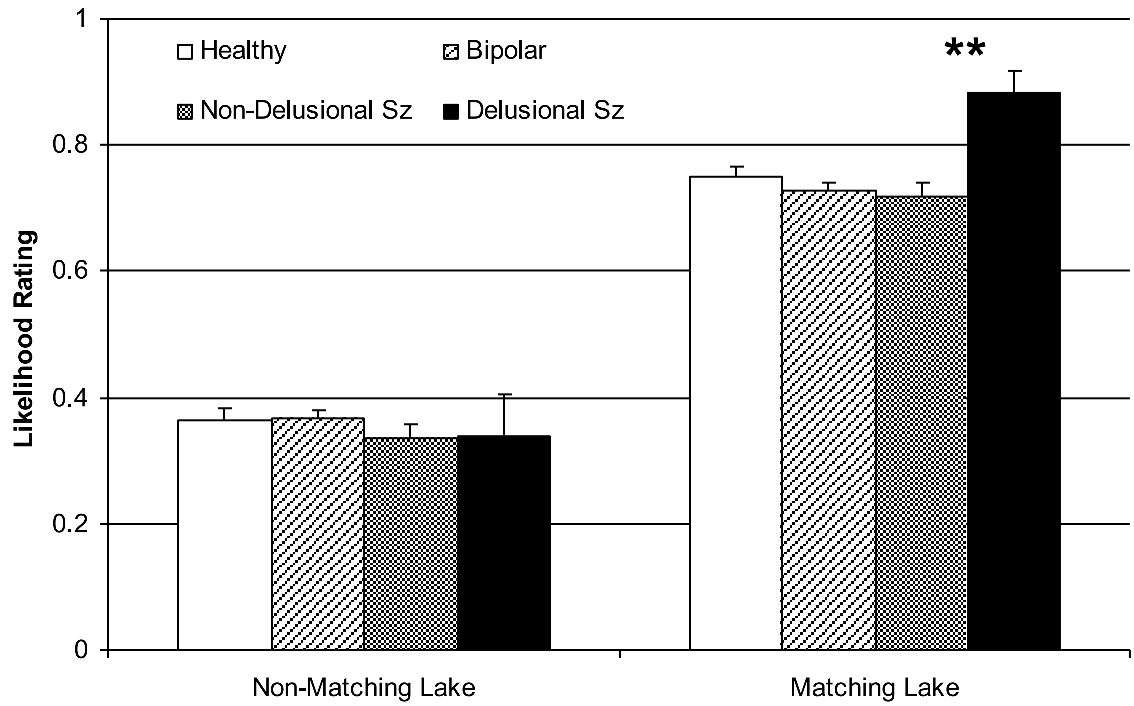
The effects of catches and series did not interact with group (all *ps* > 0.63). Therefore, we averaged group comparisons over catches and series. The group effect was significant ($F_{3,98} = 2.84$, $p < 0.05$). This effect was characterized by the ratings of the matching lake being significantly higher for the delusional schizophrenia group (mean 0.83) compared with the averaged ratings of the non-delusional schizophrenia group (mean 0.68), bipolar group (mean 0.70), and healthy control group (mean 0.69) ($F_{1,98} = 7.90$, $p <$ 0.01).

For the non-matching lake ratings, there were significant main effects of catches ($F_{9,882} = 2.62$, $p < 0.01$), and this interacted with series ($F_{9,882} = 14.13$, $p < 0.001$). The source of this interaction was that there was no significant effect of catches for Series 1 ($F_{9,882} = 1.67$, $p = 0.09$), but there was for Series 5 ($F_{9,882} = 4.20$, $p < 0.01$). The effects of catches and series did not interact with group (all *ps* > 0.07); therefore, we averaged the group comparison over catches and series. This group effect was not significant ($F_{3,98}$ = 1.54, $p = 0.21$).

2.3.3 Ratings averaged over all series

We also performed an analysis of ratings averaged over series 1–5, with separate variables computed for matching and non-matching lakes (Figure 2.5). One-way ANOVA showed a significant group effect for the matching lakes ($F_{3,98} = 4.71$, $p < 0.005$) but not for the non-matching lake ($F_{3,98} = 0.52$, $p = 0.67$). The results of *t*-tests on matching lake ratings suggested that the delusional group differed significantly from all other groups (all *ps* < 0.01), but none of the other groups differed from one another (all *ps* > 0.23). Within the whole schizophrenia group, we observed a significant correlation between the SSPI delusions item and the matching lake ratings (r[28] = 0.47, $p < 0.01$) but not for the non-matching lake ratings (r[28] = –0.04, $p = 0.83$). No comparisons were significant when the schizophrenia group was divided into patients with high and low hallucinations (all *ps* > 0.12). We could not test parallel high–low splits for other symptoms owing to the small numbers of participants with ratings in the high-to-severe range (Table 2.1).

Figure 2.5 Ratings averaged over series 1-5, plotted as a function of group and whether the presented fish matched the lake being rated. Error bars represent the standard error of the mean. ** = $p < 0.01$ for adjacent bars.



2.4 Discussion

Typically, JTC has been measured by use of the beads task, in which a single bipolar rating scale is used to measure the likelihood that beads are being drawn from one jar and not the other. Using a variant of this task, we provided separate rating scales for the two options. This approach indicated that the delusional group could be differentiated from the other groups by increased trial-by-trial likelihood ratings for whichever lake matched the current evidence. For example, if a black fish was shown, the delusions group gave a higher rating to the lake with the higher proportion of black fish than did members of the other groups. This trial-by-trial group difference was only seen for the matching lake and not for the non-matching lake. In other words, although the delusional group showed an exaggerated increase in likelihood ratings for whichever lake matched the current fish, this did not translate to correspondingly greater decreases in ratings for the lake that was not supported by the current catch. This suggests that delusions in schizophrenia are associated with a reasoning bias characterized by a “hypersalience of evidence–hypothesis matches”, but with reasoning that appears comparable to that of control groups for evidence–hypothesis non-matches. This effect was not found when we subdivided the schizophrenia group on the basis of hallucinations, suggesting that the hypersalience effect is specific to delusions.

Our results are compatible with accounts that suggest that the JTC bias is associated with delusions. Increased likelihood ratings for evidence–hypothesis matches for the delusional group may be expected to translate to a premature termination of data collection using a draws-to-decision procedure (Garety & Freeman, 1999). However, the current set of results takes the JTC theory one step further by describing why the delusional group shows a premature termination of data collection: a hypersalience of an evidence–

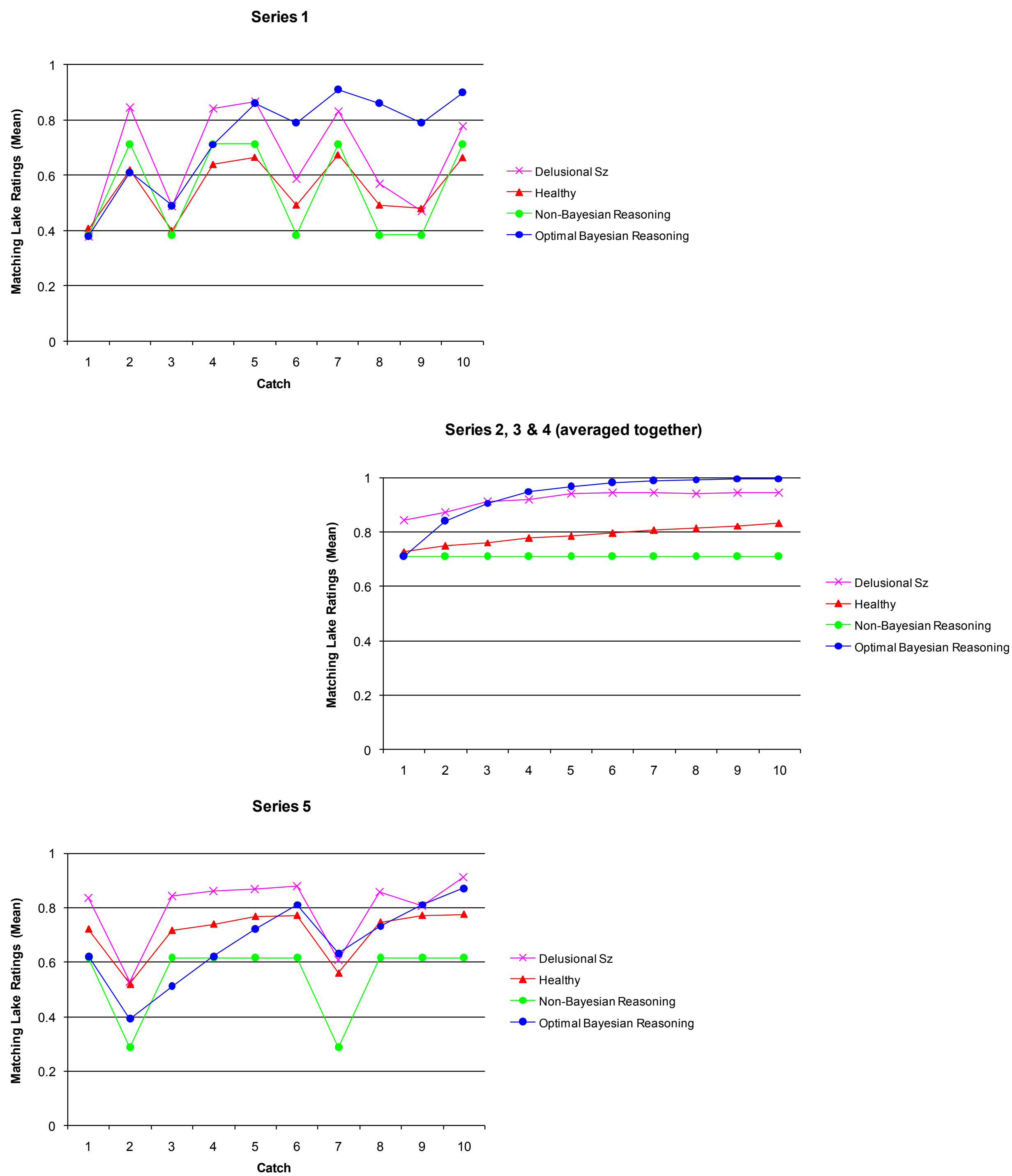
hypothesis match, which may translate into sufficient evidence for the early acceptance of an option.

Hypersalience is consistent with the aberrant salience account of psychosis (Kapur, 2003), which postulates that dysregulated dopamine transmission in schizophrenia may result in context inappropriate salience attributions, exaggerating the importance of percepts. However, to integrate this account with the current data, hypersalience must be extended only to evidence–hypothesis matches and not to any type of neutral material (notably not to evidence–hypothesis non-matches). Given that neurotransmission in the ventral striatal dopamine pathway is thought to reinforce stimulus–response or stimulus–stimulus associations (Beninger, 1983; Wise, 2004; Berridge, 2007), and, combined with the hippocampus, has the capacity to reinforce patterns of cerebral activity associated with a particular mental event (Grace, Moore & O'Donnell, 1998; Liddle, 2001), it can be speculated that evidence–hypothesis matches were hypersalient for severely delusional patients in the current study owing to dysregulated dopamine transmission in the ventral striatal dopamine pathway.

In addition to a JTC bias, the beads literature contains frequent reports of what has been referred to as either an "over-adjustment bias" (Moritz & Woodward, 2005; Langdon, Ward & Coltheart, 2010) or a "bias towards disconfirmatory evidence" (Garety, Hemsley & Wessely, 1991) in people with delusions. This effect refers to downward over-adjustments in probability estimates following a single instance of disconfirmatory evidence. Our results are directly compatible with this effect but provide an additional piece of important information: "over-adjustment" applies only to the upward rating of the matching lake or jar and not to the downward rating of the non-matching option. Thus, it is only movement towards the currently favoured option that differentiates the delusional group from the others. That such an effect is evident even on the first trial in a series, and on every trial of a series of uniform fish colours, suggests that JTC and over-adjustment may both be behaviours resulting from the hypersalience of evidence–hypothesis matches. Describing the same behaviour (high ratings on evidence– hypothesis matches) as JTC when it occurs at the beginning of a series and as over-adjustment when it occurs mid-series may be adding an unnecessary level of complexity. Put simply, our results suggest that people with delusions show a greater preference for whichever option is supported by the current incoming data, while simultaneously showing “normal” ratings for the less supported option. Whether the evidence confirms a recent judgment is irrelevant to understanding this effect.

One of the motivations for the current study was to assess how close to optimal Bayesian reasoning the different groups were. Bayesian reasoning involves the integration of incoming information with the current state of knowledge, such that the resulting probability estimates for a given trial appropriately integrate the entire series of data. At the other extreme are probability ratings that only take into account the current trial, effectively ignoring previously encountered data. This could be considered non-Bayesian reasoning in the current task. Figure 2.6 shows a comparison of responses anticipated by these two contrasting modes of responding with the actual responses of participants.

Figure 2.6 Ratings for matching lakes compared with the pattern expected if the information presented over the whole series of catches is taken into account (i.e., Bayesian reasoning), and the opposite pattern whereby individual catches are rated purely as independent events (i.e., non-Bayesian reasoning). Probabilities are computed as the probability of the focal hypothesis (i.e., the lake best supported by the fish catches or 'matching lake') being true and not the alternate hypothesis.



It has been previously suggested that the performance pattern displayed by delusional schizophrenia patients is more Bayesian than that of healthy controls (Huq, Garety & Hemsley, 1988; Maher, 1992), and therefore, more "rational" in the context of the beads task. However, as shown in Figure 2.6, it may not be completely accurate to characterize the delusional group's responses as being closer to optimal Bayesian reasoning than the other groups. For the uniform incoming data conditions, the optimal Bayesian reasoning curve shows a sharp increase in probability estimates initially, reaching a plateau after sufficient evidence has been collected. None of the groups showed this particular pattern of responding. All showed a considerably more modest influence of cumulative data across catches, with the delusional group being more confident from the outset, registering a higher baseline. The delusional group can be considered closer to optimal Bayesian responders in that their maximal level of confidence is closer to the maximal level predicted by the Bayesian formula, but, at the same time, they would be considered the least Bayesian group after only one catch, with the Bayesian formula predicting the more conservative ratings shown by the other groups.

For the mixed conditions (series 1 and 5), in which the incoming evidence is relatively less persuasive, it appears that trial-by-trial information is much more salient than series information, with the responses of all groups more closely matching the expected response for non-Bayesian reasoning, where each catch is considered an independent event. The undue influence of individual trial evidence on the ratings of all groups in a mixed condition is in accordance with past research (Fear & Healy, 1997; Moritz & Woodward, 2005). In summary, this data set suggests that it may not be accurate to describe the delusional group as being "more Bayesian" in their reasoning than the other groups.

One limitation of the current study is the very small sample size associated with the delusional group. However, achieving a modest sample of severely delusional patients would require recruitment of a very large number of people with schizophrenia, because people with this symptom profile are difficult to find. Scoring a 4 on the SSPI delusions item implies not only that a delusion is held but also that the delusion has such a pervasive influence on thinking that little else occupies the individual's thoughts. If definite delusions are present but do not have a pervasive influence on thinking, in that topics of discussion untouched by delusional thought are readily accessible, this person would rate a 3 on the SSPI delusions item. The present results suggest that these cognitive biases may only be present for delusion neutral content if delusions are very severe.

Another limitation is that other symptoms and measures of chlorpromazine-equivalent medication differed between the delusional and non-delusional schizophrenia group, although none of these were significantly different. Delusion-related symptom scores were the only variables that differed significantly between the two schizophrenia groups. The bipolar group rated lower on a number of positive symptoms than did either schizophrenia group, but since the bipolar group did not differ from the non-delusional schizophrenia group on any of the experimental measures, this would not directly affect the interpretation of the current set of results. With respect to level of medication, the direction of the medication differences were such that the performance of the more medicated group was equivalent to that of the healthy controls in all conditions, implying that higher levels of medication could not have caused the aberrant performance of those in the delusional group.

We recruited people diagnosed with bipolar disorder as a psychiatric control group. However, we were not able to recruit any bipolar participants with severe delusions. The bipolar group did not differ from the low delusions schizophrenia group for the hypersalience of evidence-hypothesis matches effect, though without a severely delusional bipolar disorder sample we are unable to comment on whether the observed effect is specific to severe delusions in schizophrenia or to severe delusions more generally.

2.5 Conclusion

In this study, a number of adaptations of previous studies appeared to clarify the source of the JTC bias observed in patients with delusions. First, we separated the ratings for lakes A and B, instead of using an integrated A–B continuous scale, allowing the observation that JTC is caused by hypersalience of evidence–hypothesis matches and does not extend to non-matching situations. This finding also suggests that it may be inappropriate to consider there to be both a JTC bias and a separate “over-adjustment” effect across trials using beads-type tasks. Second, the use of a control condition with a ratio of 50% black fish to 50% white fish allowed for the exclusion of participants using cognitive strategies that were not the target of our investigation. Third, recruitment of a sample of patients large enough to allow severely delusional patients to be grouped separately allowed for the observation of the hypersalience effect.

Chapter Three: Impaired evidence integration and delusions in schizophrenia[2]

3.1 Introduction

Much like Kuhn's (1962) views on the nature of paradigm shifts, even healthy individuals require more information to switch opinions than to form the beliefs initially. People do not vacillate upon discovery of every new piece of information. The maintenance of beliefs in the face of contradictory evidence is adaptive and necessary for consistency of thought and action. This consistency is, at least in part, maintained by a tendency to discount or reinterpret contradictory information (Nisbett & Ross, 1980). Individuals may utilise a "positive test strategy" to test hypotheses, searching for instances likely to provide confirmatory evidence (review: Klayman & Ha, 1987). This may not be the best method of truth detection, but in a real world setting where false negatives may be less costly than false positives it may often be the most adaptive approach. Friedrich (1993) uses the example of a grizzly bear: avoiding a bear that may not be dangerous based upon a general "bears are man-eaters" heuristic is safer than disregarding personal safety by approaching the bear in an attempt to falsify one's "man-eater" hypothesis. Further, positive test strategies may be beneficial for the protection of self-esteem (Friedrich, 1993). This may provide a successful default heuristic when cognitive demands are high or information is lacking, though when misapplied, can result in the erroneous judgments well documented by Kahneman's work on heuristics and biases (review: Kahneman, 2003). For example, the anchoring heuristic, which suggests that people's initial judgments can form an anchor point that biases the interpretation of subsequent information (Tversky & Kahneman, 1974)

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[2] A version of this chapter has been published. Speechley, W., Ngan, E., Moritz, S., & Woodward, T. S. (in press). Impaired evidence integration and delusions in schizophrenia. *Journal of Experimental Psychopathology*.

or the endowment effect, which indicates that people require far more to give up an object once it is obtained than they are willing to give to acquire it initially (Thaler, 1980; Tversky & Kahneman, 1991). These mechanisms may help maintain the consistency of beliefs, and in some circumstances, may result in faulty reasoning, but they are not completely inflexible; reality reigns in these biases and support sought for one's beliefs must be plausible (Kunda, 1990).

While enough contradictory evidence can accrue to cause a healthy individual to alter their views, a defining feature of delusional beliefs in schizophrenia is that they are maintained with absolute conviction despite their apparent falsehood. This feature of delusions is captured by the bias against disconfirmatory evidence (BADE; Woodward, Moritz and Chen, 2006; Woodward, Moritz, Cuttler & Whitman, 2006), which describes a maladaptive insensitivity towards evidence that should cause an individual to re-evaluate their beliefs.

In the BADE task participants are sequentially presented with three sentences that increasingly disambiguate a given scenario. After each scenario sentence is presented, participants are required to rate the plausibility of four independent interpretations of the scenario (see Table 3.1 for examples of stimuli, and Appendix I for screen shots). Two of the interpretations are initially plausible explanations that later require revision, and are referred to as lures. One option is highly implausible from the outset and remains so, and is referred to as an absurd interpretation. Finally, one is moderately plausible initially, but gradually become the most plausible, and is referred to as a true interpretation. Measurements are made of participants' willingness to adjust their plausibility ratings for the scenario interpretations as disambiguating evidence accumulates over the three statement presentations. In multiple studies BADE has been shown to be a robust effect in schizophrenia (Moritz & Woodward, 2006; Woodward, Moritz, Menon & Klinge, 2008), with some data suggesting that the effect is stronger for delusional patients (Woodward, Moritz and Chen, 2006; Woodward, Moritz, Cuttler & Whitman, 2006).

Table 3.1 Examples of BADE stimuli

Example	Scenario Statements	Interpretations
1	Nicholas is driving his car very fast Nicholas did not stop at the red light Nicholas injured a little girl with his car	Nicholas is running late for work (L) Nicholas' wife is in labour (L) Nicholas hates going for walks (A) Nicholas is a hit and run offender (T)
2	Amanda is very thin Amanda has a difficult life Amanda doesn't even have a home	Amanda is a runway model (L) Amanda has an eating disorder (L) Amanda has lost her fake teeth (A) Amanda is homeless (T)
3	The woman has been in severe pain all day The woman is impatiently waiting for her special day to come The woman has a big belly	The woman is training to be a champion gymnast (L) The woman has only days left to live (L) The woman loves to be tickled (A) The woman is about to have a baby (T)
4	Mark often comes home late from work Mark tells his wife that he is not in the mood to spend time with her Mark's wife is suspicious	Mark is trying to earn a promotion at work (L) Mark must work hard in order to not lose his job (L) Mark thinks that money grows on trees (A) Mark is having an affair (T)

(T) = True; (L) = Lure; (A) = Absurd

In earlier research the BADE effect was most often operationalized as the degree of reduction in plausibility ratings for "lure" interpretations, which appear plausible initially, but are rendered implausible as incoming evidence clarifies the scenario (Woodward, Moritz, Cuttler & Whitman, 2006; Moritz & Woodward, 2006; Woodward, Moritz and Chen, 2006; Woodward, Moritz, Menon & Klinge, 2008; Buchy, Woodward & Liotti 2007). These conclusions were based on univariate analyses, and therefore did not consider information available from overlap between the BADE items. The use of all available measures can simplify interpretations of test performance by considering overlap and redundancy between test items to determine the nature of the cognitive operations underlying all responses. Previously, using data from a healthy group of university students screened for schizotypal traits, a multivariate analysis on BADE lure items and a number of traditional neuropsychological measures determined that only two cognitive operations contributed to the lure rating scores (Woodward, Buchy, Moritz & Liotti, 2007). We labeled these "Initial Belief" (composed of lure ratings after statement one) and "Integration of Disconfirmatory Evidence" (composed of lure ratings following statement three). This suggested that the BADE task engages two independent cognitive operations; one subserving initial responses, when a paucity of information generates greater ambiguity, and one underpinning responses towards the end of the task, once sufficient evidence has been provided to allow greater discrimination between the response options. Only the Integration of Disconfirmatory Evidence component was associated with delusional ideation on the Schizotypal Personality Scale (SPQ) (Raine, 1991).

To date, all previous BADE theorizing has focused on the lure items alone, either using univariate analysis on change scores or multivariate analysis on lure ratings. The goal of the current study was to use all items (true, absurd and lure) in a multivariate analysis to allow all ratings to contribute to the interpretation of the cognitive underpinnings of the evidence integration necessary in the BADE task. Additionally, no previous studies have conducted multivariate analyses on BADE task data collected from patient groups. To this end, we recruited a schizophrenia group and a sample of people diagnosed with bipolar disorder, as a psychiatric control group. Based on the analysis of the schizotypy data, collected from healthy university students (Woodward, Buchy, Moritz & Liotti, 2007), we anticipated that two cognitive factors would emerge from all BADE items, and that a diagnosis of schizophrenia with severe delusions would result in the most impairment in evidence integration. Healthy controls were expected to show the least evidence of a BADE, and schizophrenia with mild/no delusions and bipolar disorder falling in between.

3.2 Methods

3.2.1 Participants

Fifty people with a diagnosis of schizophrenia and 60 people with a diagnosis of bipolar disorder were recruited from psychiatric hospitals and community health agencies in and around Greater Vancouver, British Columbia, Canada. All diagnoses were made by ward psychiatrists and, if in doubt, confirmed using a neuropsychiatric interview (MINI; Sheehan, Lecruibier and Sheehan, 1998) conducted by trained research staff. Psychopathology was assessed using the Signs and Symptoms of Psychotic Illness scale (SSPI) (Liddle, Ngan, Duffield, Kho & Warren, 2002), a schedule gauging symptom severity using 20 symptom items scored 0–4. As with our previous work (Speechley, Whitman & Woodward, 2010) the SSPI Item 7 was used to separate out a severely delusional schizophrenia group (n = 10) from the mild/no delusions schizophrenia group (n = 40) (delusions item = 4, and < 4, respectively). T-tests indicated no between-group differences for age of onset of schizophrenia, length of illness, age first hospitalised or number of hospitalisations. The bipolar group rated low for delusions with 42 participants scoring a zero, 13 receiving a rating of one, and five a rating of two for the SSPI delusions item. Patients who met the DSM-IV criteria for substance abuse and dependence, a history of serious head injury, neurological illnesses requiring treatment, or other Axis I diagnoses were excluded from participation in this study. With the exception of one individual, all participants diagnosed with schizophrenia were stabilized with neuroleptic medications, with the large majority taking atypical neuroleptics. Of the patients in the bipolar group, 21 of 55 were taking atypical neuroleptics, while the remainder were not taking any antipsychotic medication. Chlorpromazine equivalents are presented in Table 3.2.

Forty-four healthy controls were recruited through advertisement and word-of-mouth. Screening with a medical questionnaire ensured that none of the healthy participants had any current or prior history of psychiatric illness. Additional exclusion criteria were the same as those employed for the patient groups.

All participants were fluent in English, used English daily, and had been speaking English daily for at least the past five years. Prior to participation in the BADE task, intelligence estimates were made using the Kaufman Brief Intelligence Test (K-BIT; Kaufman & Kaufman, 1990) for current verbal and non-verbal intelligence, and the Ammons Quick Test (QUICK; Ammons & Ammons, 1962) for a proxy assessment of premorbid IQ. The K-BIT takes approximately 20 minutes to administer and includes a verbal and a non-verbal intelligence scale, as well as providing a composite IQ score. The verbal scale includes word knowledge, verbal concept formation, and reasoning ability, while the non-verbal scale includes a matrices subtest. The QUICK takes approximately five minutes to administer and requires participants to indicate which of four pictures best fits the meaning of a series of words spoken aloud by the experimenter. Socio-economic status was estimated using the Hollingshead Two-Factor Index of Social Position (Hollingshead, 1957) using highest parental occupation and education level. Sociodemographic characteristics of the sample are summarized in Table 3.2, and any significant between-groups differences on these variables are flagged. Where significant between-groups differences were found, those variables were covaried out of the main effects of interest using analysis of covariance (ANCOVA).

Table 3.2 Sociodemographic characteristics of the samples: means, with standard deviations in parentheses.

	Healthy controls (n = 44)	Bipolar (n = 60)	Non-delusional Sz (n = 40)	Delusional Sz (n = 10)
Age	35.39 (11.37)	41.62 (10.05)††¶¶	35.36 (11.78)	41.10 (12.19)
Sex (M:F)	17:27‡	27:33††	30:10	5:5
Years of Education	14.52 (2.21)§‡‡	14.90 (3.48)*†††	12.33 (2.86)	12.00 (1.89)
Length of illness	n/a	14.64 (11.07)	13.00 (10.87)	20.33 (10.36)
K-BIT vocab	100.48 (15.66)	105.47 (17.00)*††	93.97 (11.81)	90.33 (12.03)
K-BIT matrices	98.88 (22.37)	97.44 (12.69)	94.86 (14.33)	94.00 (19.07)
K-BIT composite	99.73 (17.69)	100.86 (11.53)*††	93.97 (12.63)	91.67 (16.85)
QUICK	102.60 (11.68)	108.42 (11.33)*†¶	103.42 (11.58)	98.67 (8.19)
Social status	35.74 (16.44)	31.21 (17.35)	33.71 (16.09)	42.33 (19.59)
Chlorpromazine Equivalent (mg)	n/a	110.05 (479.27)	230.59 (352.29)	301.88 (186.51)

*Delusional schizophrenia vs. bipolar, $p < 0.05$; §Delusional schizophrenia vs. healthy, $p < 0.01$; †Non-delusional schizophrenia vs. bipolar, $p < 0.05$; †† Non-delusional schizophrenia vs. bipolar, $p < 0.01$; ††† Non-delusional schizophrenia vs. bipolar, $p < 0.001$; ‡Non-delusional schizophrenia vs. healthy, $p < 0.01$; ‡‡Non-delusional schizophrenia vs. healthy, $p < 0.001$; ¶Bipolar vs. healthy, $p < 0.05$; ¶¶Bipolar vs. healthy, $p < 0.01$

3.2.2 Procedure

The BADE test was conducted in a testing room at the University of British Columbia using Microsoft Internet Explorer 6.0. An experimenter was present throughout the entire procedure. The BADE test used 30 delusion-neutral scenarios (Buchy, Woodward & Liotti, 2007; Woodward, Buchy, Moritz & Liotti, 2007). Twenty-four of the BADE scenarios were expressed in the form of three sequentially presented and increasingly disambiguating sentences describing a delusion-neutral scenario. For example, one of the scenarios described a girl who cannot fall asleep on Christmas Eve because, as becomes increasingly apparent, she is eagerly anticipating Santa Claus bringing Christmas presents later that night. The first sentence presented for this scenario was, “Jenny can't fall asleep”. For this scenario, the four interpretations that must be rated for plausibility were: one “true” interpretation (e.g., “Jenny is excited about Christmas morning”), two “lure” interpretations (e.g. “Jenny is nervous about her exam the next day” and “Jenny is worried about her ill mother”), and one absurd interpretation (e.g., “Jenny loves her bed”). Note that the “true” interpretation would not be considered particularly plausible after the first sentence describing the scenario. The second sentence presented was, “Jenny can't wait until it is finally morning”, and the third was, “Jenny wonders how many presents she will find under the tree”. After the third sentence has been presented, the scenario should be clear to the participants, indicating that the lures should be down-rated, and the true interpretation up-rated. Thus, the true interpretation appeared to be less plausible initially, though became increasingly plausible with each successive piece of confirmatory evidence, while the two lures initially appeared to be plausible, but became increasingly less plausible. The absurd interpretation was designed to be implausible even from the presentation of the initial sentence. An additional series of events is depicted in screen shots in Appendix I, with further BADE trial examples given in Table 3.1.

Plausibility ratings were recorded on a 0-10 rating scale using a scroll bar positioned beneath each interpretation. The nominal ratings “Poor”, “Possible”, “Good”, and “Excellent” were evenly distributed along the scale. Ratings were made and adjusted via mouse click. To avoid participants settling into one pattern of responding, the remaining six of the 30 scenarios were “distracters”. For these stimuli the true answer was apparent following the very first piece of evidence. The sentences for this task were chosen and constructed based on extensive piloting, and were previously rated by 69 undergraduate students (Buchy, Woodward & Liotti, 2007; Woodward, Buchy, Moritz & Liotti, 2007), confirming the desired lure/absurd/true pattern.

Prior to testing, the experimenter described the rating scale to participants, indicating that each of the interpretations were independent, and that ratings could be changed after the presentation of each piece of information. One practice trial was given to familiarize participants with the procedure.

3.2.3 Data analysis

In order to consider overlap and redundancy between test items, and to determine the number of cognitive operations underlying all responses, we submitted all 12 plausibility ratings (four rating types - one true, two lure and one absurd interpretation - each rated three times) to a principal component analysis (PCA). We planned a Group (schizophrenia, severely delusional schizophrenia, bipolar disorder, and healthy controls) by Component (a two-component solution was expected) mixed-model ANOVA.

Significant main or interaction effects were followed up using univariate ANOVAs and *t*-tests.

3.3 Results

3.3.1 Principal component analysis (PCA)

The BADE test variables (mean plausibility ratings for true interpretations, absurd interpretations and both lures following each of the three pieces of evidence; Table 3.3) for all participants were entered into a PCA with oblimin rotation. The scree plot and Kaiser-Guttman criterion (eigenvalues > 1) converged on a clear two-component solution (eigenvalues: 7.06, 3.10, 0.72, 0.46, 0.24, 0.13, 0.11, 0.08, 0.04, 0.03, 0.02 and 0.02), which accounted for 85% of the total variance. Component pattern weights for the total sample are listed in Table 3.4 (the same analysis carried out on each subsample is also listed in order to demonstrate the reliability of the solution). The rotation sums of squares loadings showed that Component 1 accounted for 46.96% of the total variance, and that the rotated Component 2 accounted for approximately 46.03% of the total variance (these percentages are over-additive due to the non-orthogonal rotation). This suggests that all BADE ratings can generally be interpreted within the context of two cognitive operations. Component 1 was dominated by plausibility ratings for all absurd interpretations, lure interpretations following sentence two and, in particular, sentence three, and true interpretations on rating three (loaded negatively). Component 2 was dominated by ratings for lure and true interpretations after receiving the first and second pieces of evidence, as well as the true interpretation on rating three (loaded positively).

Table 3.3 Mean plausibility ratings for all BADE test variables following each of the three pieces of evidence; means, with standard deviations in parentheses

Statement	Delusional Sz	Schizophrenia	Bipolar	Healthy Control
Absurd One	2.59 (2.32)	1.65 (1.30)	1.67 (1.30)	1.05 (0.82)
Absurd Two	2.83 (2.34)	1.41 (1.15)	1.35 (1.19)	0.71 (0.66)
Absurd Three	2.44 (2.33)	0.88 (1.10)	0.94 (1.09)	0.33 (0.49)
Lure A One	5.45 (2.12)	5.14 (2.15)	4.95 (2.05)	4.60 (2.05)
Lure A Two	4.66 (2.24)	3.96 (1.79)	3.41 (1.50)	3.34 (1.58)
Lure A Three	3.15 (2.65)	1.97 (1.98)	1.45 (1.23)	1.15 (1.28)
Lure B One	5.34 (2.24)	4.67 (2.14)	4.66 (2.03)	4.22 (1.96)
Lure B Two	4.67 (2.27)	3.70 (1.73)	3.56 (1.63)	3.28 (1.43)
Lure B Three	3.46 (2.59)	1.85 (1.82)	1.63 (1.46)	1.14 (1.29)
True One	5.19 (2.47)	4.82 (2.12)	4.71 (2.01)	4.34 (1.94)
True Two	6.48 (2.49)	6.54 (2.12)	6.58 (1.93)	6.36 (1.74)
True Three	8.24 (2.34)	9.07 (1.36)	9.09 (1.55)	9.40 (0.68)

Table 3.4 Pattern weights for BADE variables (*N* = 149). The participants were comprised of a schizophrenia group (*n* = 50), a psychiatric control group (*n* = 60) and a healthy control group (*n* = 44).

	Component							
	1 Evidence Integration				**2** Believability			
Statement	T	S	B	C	T	S	B	C
Absurd one	**.775**	**.796**	**.798**	**.532**	.291	.264	.300	**.446**
Absurd two	**.908**	**.900**	**.926**	**.835**	.098	.114	.097	.090
Absurd three	**.961**	**.977**	**.958**	**.911**	-.116	-.135	-.098	-.245
Lure A one	.185	.278	.123	.075	**.895**	**.835**	**.928**	**.941**
Lure A two	**.552**	**.656**	**.529**	**.441**	**.641**	**.541**	**.692**	**.716**
Lure A three	**.901**	**.952**	**.868**	**.875**	.014	-.117	.094	.023
Lure B one	.088	.165	.008	.037	**.939**	**.890**	**.973**	**.963**
Lure B two	**.533**	**.626**	**.495**	**.420**	**.628**	**.543**	**.653**	**.724**
Lure B three	**.882**	**.925**	**.878**	**.860**	.009	-.066	-.023	.059
True one	.088	.130	.041	.045	**.942**	**.920**	**.960**	**.952**
True two	-.141	-.071	-.248	-.059	**.965**	**.963**	**.957**	**.946**
True three	**-.584**	**-.462**	**-.684**	**-.426**	**.645**	**.729**	**.553**	**.758**

Note: All pattern weights over 0.40 are set in bold font. Component solutions are presented for total sample and subgroups separately. T = total sample; S = schizophrenia group; B = bipolar group; C = healthy control group.

An important factor for labeling and distinguishing between the components is the third rating for the true interpretation, which loads strongly on both components, but in opposite directions. For Component 1, these negative loadings indicate that people rating high for lures rate low for trues, and vice-versa, indexing the degree to which they have fully integrated the disambiguating evidence; thus, this component was labeled "Evidence Integration". For Component 2, none of the absurd items loaded, while all of the true items did. Both lures loaded on Component 2 for ratings one and two, though not for rating three. As a broad rule, all items that were designed to receive relatively high ratings loaded onto this component, while none of the items that were expected to receive low ratings loaded. Hence, Component 2 was labelled "Believability". Split-half reliability computed on the components described above (24 BADE items randomly split into two sets of 12) was exceptionally high, with a Pearson's correlation coefficient of 0.94 for Believability and 0.93 for Evidence Integration. The two components were correlated at 0.25.

3.3.2 Group by component analysis

The component scores for Evidence Integration and Believability were entered into a repeated measures ANOVA to determine whether they were able to discriminate the severely delusional schizophrenia group from the other groups. This analysis revealed a significant interaction of Group membership with Component, $F(3,149) = 3.77$, $p < 0.05$, reflecting a significant Group effect for Evidence Integration, $F(3,149) = 8.24$, $p < 0.001$, but no significant Group effect for Believability $F(3,149) = 0.21$, $p = 0.88$.

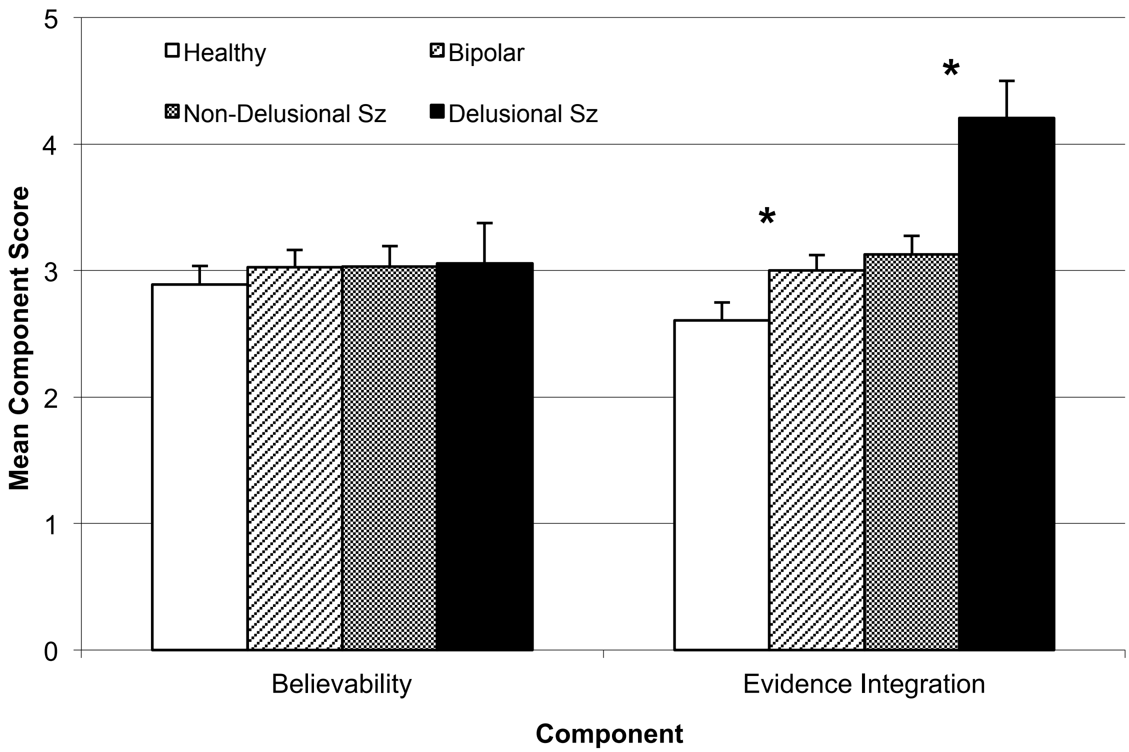
Between groups *t*-tests for Evidence Integration indicated that the severely delusional schizophrenia group (M = 1.20) had significantly higher component scores than the other schizophrenia group (M = 0.12), $t(47) = 2.58$, $p < 0.05$, the bipolar group (M =

0.00), $t(68) = 3.23$, $p < 0.01$, and the healthy control group (M = -0.39), $t(52) = 5.07$, $p < 0.001$. Both the schizophrenia group, $t(81) = 2.94$, $p < 0.01$, and the bipolar group, $t(102) = 2.49$, $p < 0.05$, had significantly higher Evidence Integration component scores than the healthy control group, though were not significantly different from each other. These relationships are presented in Figure 3.1.

ANCOVAs for demographic items for which significant group differences were found (Table 3.2) showed that the between groups differences on Evidence Integration remained significant when these variables were covaried out (Age, $F(3,149) = 7.76$, $p < 0.001$; K-BIT Vocabulary, $F(3,149) = 6.04$, $p = 0.001$; K-BIT Comprehensive, $F(3,149) = 6.44$, $p < 0.001$; QUICK, $F(3,149) = 8.95$, $p < 0.001$; Years of Education, $F(3,149) = 8.46$, $p < 0.001$).

The specificity of the Evidence Integration component as a discriminator between the schizophrenia group and severely delusional schizophrenia group was examined by repeating the analysis described above for high and low hallucinations, and high and low formal thought disorder, using comparable subdivisions of the same schizophrenia patient sample. Neither Evidence Integration nor Believability differed between high and low subgroups for hallucinations (all *p*s > 0.13) or formal thought disorder (all *p*s > 0.12).

Figure 3.1 Mean component scores (Believability and Evidence Integration) plotted as a function of group (healthy controls (n = 44), psychiatric controls (n = 60), non-delusional schizophrenia patients (n = 40) and delusional schizophrenia patients (n = 10)). The mean of the component scores was rescaled to three for display purposes.



* $p < 0.05$ for adjacent bars.

3.4 Discussion

Two components accounted for 85% of the variance in the BADE task: Evidence Integration (plausibility ratings reflecting the degree to which disambiguating information has been integrated) and Believability (plausibility ratings for items designed to be given relatively high ratings). Only Evidence Integration scores differed between the severely delusional schizophrenia group and the other schizophrenia group; Believability scores did not differ, arguing against a generalized task performance deficit. Delusions were associated with higher Evidence Integration scores, reflecting comparatively higher plausibility ratings for disconfirmed interpretations, combined with lower ratings for confirmed (true) interpretations, indicating a reduced tendency to adjust beliefs when confronted with disambiguating evidence. The opposite was true for the healthy control group, who showed more complete evidence integration than any of the patient groups.

The two components derived from the PCA of the previous BADE study on healthy subjects agreed with those reported here (Woodward, Moritz, Menon & Klinge, 2008), but because only lure items were analyzed in that study, the selection of component labels did not benefit from observation of how true and absurd items load onto the components along with the lures. In the previous study, Component 1 was labelled “Integration of Disconfirmatory Evidence”, but due the high involvement of the absurd items, and the negative loadings on the true items, we changed the name to Evidence Integration (that is, integration of disambiguating evidence, disconfirmatory or otherwise). In the previous study, Component 2 was labelled “Initial Belief”, but due the high involvement of the true items on ratings two and three we renamed this component “Believability”.

The relationship between BADE and JTC deserves particular consideration in that JTC research using the “beads task” has reported what has been referred to as either an "over-adjustment bias" (Moritz & Woodward, 2005; Langdon, Ward & Coltheart, 2008) or a "bias towards disconfirmatory evidence" (Garety, Hemsley & Wessely, 1991) in people with delusions. A bias towards disconfirmatory evidence has been suggested due to evidence of downward over-adjustments in probability estimates following a single instance of disconfirmatory evidence in the beads task, while with the BADE task, we suggest that there is a bias against disconfirmatory evidence, such that judgments are not adjusted downwards sufficiently once information contradicting the initial judgment is presented. Both effects appear robust and have been frequently replicated, though provide contradictory explanations of the responses of people with delusions to disconfirmatory evidence.

In Chapter Two data was presented enabling a reconsideration of the disconfirmatory bias demonstrated in the JTC-beads literature (Speechley, Whitman & Woodward, 2010). Previous beads task research has employed a single rating scale with choice A at one end of the scale and choice B at the other. With this measurement scale it is impossible to know whether a movement in one direction represents a downward rating adjustment for one option, an upward rating for the other, or both. In Chapter Two, a separate rating scale was employed for each of the two response options allowing for the observation that when a piece of evidence was presented that was contrary to the previous piece of evidence the delusions group showed a greater increase in probability estimates for the option that best matched the current evidence, though did not show a commensurately larger decrease in ratings for the option not supported by the new evidence. Since it appears that the previously reported over-adjustment applies only to the upward rating of the matching option, the previous characterisation of this effect as a "disconfirmatory bias" may be somewhat inaccurate. Further, it appears that it is unnecessary to consider there to be a JTC effect at the beginning of a series of bead draws, and a separate disconfirmatory bias evidence during later draws. Unlike JTC, a hypersalience of evidence-hypothesis matches explanation suggests that the effect does not only occur at the beginning of a trial, but occurs at any point new evidence is provided.

The work in Chapter Two may have offered further information on the JTC and disconfirmatory biases described in the beads literature, however, this does not directly address the disconnect between a tendency to adopt or switch beliefs on the basis of little evidence and the tendency to tenaciously hold on to a belief despite its poor correspondence with the available evidence. It may be that the hypersalience of evidence-hypotheses matches/JTC contributes to the formation of delusional beliefs, while BADE may be best understood as a bias contributing to delusion maintenance. These may be independent biases identified by virtue of methodological differences between the two tasks.

This study is subject to a number of limitations. First, the sample size for the severely delusional schizophrenia group is small. However, the ability to detect the effects reported here depended upon procuring a relatively large sample of people diagnosed with schizophrenia (N = 50), such that a subgroup of patients with the most severe delusion symptoms could be split off from the rest of the group. In all previous BADE studies, total sample sizes for the schizophrenia group were smaller, requiring lower cut-offs for inclusion in the delusion group in order to allow reasonable subgroup sample sizes. Lower cut offs resulted in the averaging together of patients experiencing milder levels of delusions with those experiencing severe delusions, perhaps accounting for some of the inconsistency previously reported when investigating whether a BADE effect is more pronounced in a delusional schizophrenia group compared to a non-delusional group.

As with the study presented in Chapter Two, we were unable to recruit a severely delusional bipolar disorder sample. Both the bipolar group and low delusions schizophrenia group showed greater evidence of BADE than the healthy control group, with similar levels of BADE to each other (as indexed by Evidence Integration scores). However, without a severely delusional bipolar sample it is not possible to comment on whether the highest levels of BADE, shown by the severely delusional schizophrenia group, is specific to severe delusions in schizophrenia or to severe delusions more generally.

Another potential limitation of this study is that there were a number of differences observed between the groups on demographic variables. Despite using ANCOVA to ensure that these differences did not impact the main results, ideally all groups would be matched on all demographic variables. However, in this regard it is important to note that the key group comparison, the schizophrenia group versus severely delusional schizophrenia group, was not affected by this limitation, as these two groups did not differ significantly on any demographic variables.

3.5 Conclusion

The results of this study support the notion that the BADE task may engage two distinct cognitive processes, though only the Evidence Integration component, which requires the consideration or reconsideration of beliefs in light of disconfirmatory evidence, appears to discriminate between the severely delusional schizophrenia group and other psychiatric patient groups. Evidence integration and BADE have been incorporated as treatment targets in metacognitive training (MCT; Moritz et al. 2005, 2007; Moritz & Woodward, 2007). MCT is designed to provide patients with knowledge of their metacognitive infrastructure (e.g., reasoning biases such as BADE), and provides exercises and experience in correcting cognitive biases. Increased awareness of the role of Evidence Integration in reasoning may help protect against delusional ideation in schizophrenia.

Ultimately, this study provides further confirmation that the cognitive biases in delusions extend beyond material congruent with an individual's specific delusions to neutral, unrelated content, and as such, may reflect a pervasive reasoning deficit predisposing towards the formation and maintenance of delusional ideation.

Chapter Four: Dual-stream modulation failure: A novel hypothesis for the formation and maintenance of delusions in schizophrenia[3]

4.1 Introduction

Delusions are one of the cardinal and arguably most debilitating symptoms of schizophrenia. They range from bizarre forms, such as alien thought insertion, to more theoretically plausible non-bizarre forms, such as a belief in government surveillance, and can be either mood-congruent or mood-incongruent. Given the particular problems in satisfying the falsity stipulation of the DSM definition, the hallmark of delusional beliefs can be considered to be their persistence in the face of overwhelming contradictory evidence. It is this feature that sets them apart from normal erroneous beliefs, and it is this feature that sets them apart from normal psychology, moving delusional belief systems into the realm of psychiatric and medical pathology.

Research presented in chapters two and three replicate and extend knowledge on two previously identified cognitive biases in schizophrenia: the circumscribed approach to evidence evaluation described by JTC, previously suggested to contribute to delusion formation, and the suboptimal evidence integration described by BADE, which may be a factor in delusion maintenance. Now that it has been established that there are cognitive biases that can be detected outside of the circumscribed domain of an individual's delusional beliefs, we attempt to elucidate the mechanisms that may underlie the aberrations in reasoning that may contribute to delusional ideation.

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[3] A version of this chapter has been published. Speechley, W., & Ngan, E (2008). Dual-stream modulation failure: A novel hypothesis for the formation and maintenance of delusions in schizophrenia. *Medical Hypotheses, 70*, 1210–4.

4.2 The dual-stream modulation failure model of delusions

The acceptance of erroneous beliefs despite convincing counter evidence represents a fundamental error in decision-making. Dual-stream processing models are well developed in other scientific branches, including psychology, game theory, and commerce. However, despite their potential to further our understanding of delusions, dual-stream models have yet to be modified and applied to schizophrenia. Dual-stream models divide decision-making into two separate, but interacting processes: an experiential, intuitive, associative stream and a rational, sequential, logical stream. Given that people with delusions appear able to hold an irrational belief while simultaneously being aware of the compelling evidence to the contrary, we propose that dysfunctions in the normal interaction and integration of these two streams can account for this key feature of delusions, providing a testable mechanism for their formation and maintenance.

Colloquially, the two streams of processing can be expressed as those decisions made by the "heart" or "gut" versus those made by the "head" (Epstein, 1994). In the decision-making literature, the terminology for the two streams varies quite dramatically (Table 4.1), though the essential flavour remains the same. For this reason, we have adopted the neutral umbrella terms Stream 1 and Stream 2 (adapted from Stanovich & West, 2000) to refer to the intuitive and deliberative streams, respectively. Stream 1 carries out an associative form of analysis that is fast and effortless, occurring somewhat automatically and without the need for careful consideration. This process is associative in the sense that assessments are the product of comparisons with past experiences or knowledge, and may be guided by habit (Kahneman, 2003). Stream 2 is a conscious, sequential process that is relatively slower and requires greater effort. This places it in the domain of rule-based, analytical inference (Kahneman, 2003). In short, Stream 1 is a “reflexive” mode of decision-making, while Stream 2 is more “reflective” (Lieberman, Gaunt, Gilbert & Trope, 2002).

Table 4.1 Summary of dual-stream processing terminology (adapted from Epstein (1994) and Kahneman (2003)).

	Stream 1	**Stream 2**
Descriptors	Intuition	Reason
	Instinct	Logic
	Impression	Propositional Thought
	Schemata	Thoughtfulness
	Gut Feeling	Working Memory
	Natural Assessment	Permissive Monitoring
	Narrative Thought	Doubt
	Prototype Heuristics	Deliberation
Properties	Fast/Rapid	Slow
	Associative	Rational
	Unintentional	Intentional/Deliberate
	Effortless/Automatic/Passive	Effortful
	Implicit/Non-verbal	Explicit/Verbal
	Governed by habit	Sequential/Serial
	Preconscious	Conscious/Self-Monitored
	Inflexible	Flexible
	Concrete	Abstract/Conceptual
	High Accessibility	Rule Governed
	Emotional/Affective	Neutral
	Experiential	Corrective
	Unreflective/Reflexive	Reflective
	Primitive	Complex
	Action Oriented	Analytic
	Holistic	Controlled
	Imaginistic	Extensional

Although dual-stream processing accounts consider two separate modes of processing, the two streams are not completely disparate, and are believed to operate reciprocally, governing all decision- making processes in parallel (Epstein, 1994). The effortlessness of Stream 1 processing imbues it with a high level of accessibility, such that it tends to subconsciously control judgments unless they are modified or overridden by conscious, deliberative reasoning (Epstein, 1994; Kahneman, 2003). Kahneman (2003) suggests that a judgment begins with an intuition that is then endorsed, adjusted, corrected or blocked by Stream 2. If there is no intuitive response at all, the entire judgment is computed by Stream 2. We propose two key dual-stream modulators that determine the degree of influence each stream exerts over decision-making in a given context: conflict and emotion (Figure 4.1a). We suggest that delusional ideation in schizophrenia may be the result of a failure of either or both of these dual-stream modulators (Figure 4.1b).

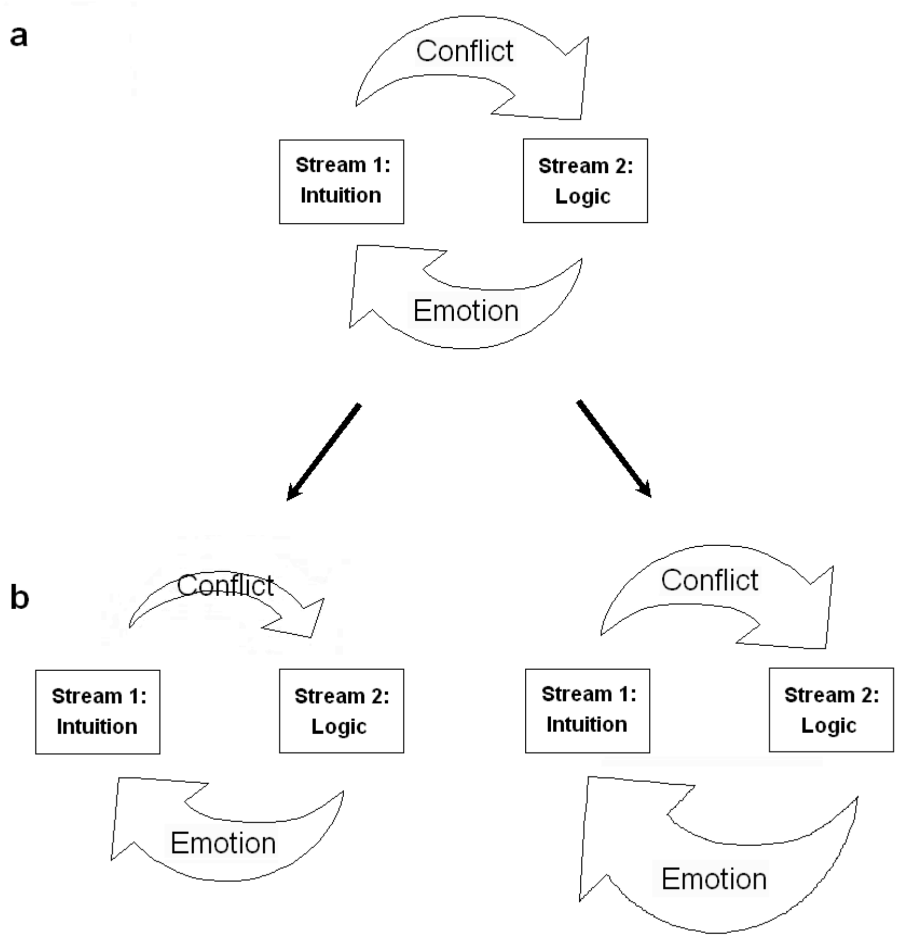

Figure 4.1 The Dual-Stream Modulation Failure model of delusion formation and maintenance. (a) In healthy individuals, judgments are the product of a dynamic interaction between an intuitive and a logical stream of reasoning. This system is influenced by two key biases: conflict and emotion. When there is a conflict between the two streams, the detection of this conflict biases reasoning towards the slower and more reflective Stream 2. Under emotionally salient conditions there is a bias towards the more automatic and reflexive Stream 1. (b) Abnormalities in either or both of these decision-making biases provide a mechanism that can account for the formation and maintenance of delusions in schizophrenia. *Left:* A failure of conflict to modulate decision-making may allow divergent Stream 1 and Stream 2 judgments to coexist without the need for reconciliation. *Right:* Emotional stimuli may be aberrantly salient for people with delusions (especially for material relating to delusion content), inducing a more powerful Stream 1 bias, and further attenuating the accessibility of competing information.

4.2.1 Conflict-modulation failure

Delusions are a state in which a belief is firmly held despite all evidence to the contrary. Why does convincing counter evidence fail to persuade delusional individuals of the fallaciousness of their beliefs? Within the dual-stream processing model a belief can be viewed as the result of either a rapid, associative Stream 1 process or a slower, more deliberate, Stream 2 procedure. In most situations these two processes converge onto the same solution, though it is not unusual for divergence to occur, leading to the proverbial conflict between the "head" and the "heart". When Stream 1 and Stream 2 decisions diverge, healthy individuals should experience dissonance, or a sense of conflict. We propose that, in healthy individuals, this conflict biases decision-making towards Stream 2 processing (Figure 4.1a), initiating a more thorough consideration of the available evidence. Syllogistic reasoning tasks provide a good demonstration of the manner in which the two streams can conflict during decision-making. For example, in the syllogism, "All birds fly. Pigs are birds. Pigs fly", the final statement is unbelievable, but the syllogism is logically valid. This results in an automatic, believability driven assessment of validity that conflicts with the deliberative task requirement to determine the syllogism's logical validity. The experience of this conflict should initiate a bias towards Stream 2, increasing the likelihood that the Stream 1 appraisal will be suppressed and the syllogism judged logically valid. We suggest that, in schizophrenia, a conflict modulation failure reduces the influence of contradictory evidence on decision-making resulting in a failure to correct erroneous beliefs (Figure 4.1b). This proposal is supported by evidence that, compared to healthy controls, people with schizophrenia show reduced activity in regions of the brain associated with conflict detection (e.g., anterior cingulate cortex) when viewing incongruent stimuli in the Stroop task (Carter, Mintun, Nichols & Cohen, 1997), and in response to error commission during Go/No Go tasks (Laurens, Ngan, Bates, Kiehl & Liddle, 2003).

4.2.2 Accentuated emotional modulation

Real world decision-making is intimately entwined with emotion. Therefore, for a model of decision-making to be complete, this element must be considered. Damasio's Iowa Gambling Task research on the somatic marker hypothesis demonstrates the importance of affect in eliciting physiological responses essential for approach and avoidance learning in decision-making (1994; Bechara, Damasio, Damasio & Anderson, 1994; Bechara, Damasio, Tranel & Damasio, 1997; Damasio, Tranel & Damasio, 1991). However, while appropriate emotional responses may be essential for effective learning and decision-making in some circumstances, emotion may need to be inhibited to avoid irrational responses during the more abstract and socially complex decision-making required in modern society (Greene et al., 2004; De Martino, Kumaran, Seymour & Dolan, 2006). This is well evidenced by the framing effect (Kahneman & Tversky, 1979; Tversky & Kahneman, 1981), which demonstrates how emotions can bias decision-making. The framing effect is a change of preferences between options dependent on whether a scenario is framed in terms of losses or gains. For example, one study examined the effects of framing on treatment choice (surgery versus radiation therapy for cancer patients), where the long term (five year) survival for surgery was superior to that of radiation therapy, but where the surgery was associated with higher immediate risks, including a 10% chance of dying from the surgery itself. The percentage of patients choosing surgery, which offered a better long-term health outcome, depended on how the information was framed. When framed in a percentage survival context (90 % survive the operation and 34 % survive after five years, compared to 100% survive radiation and 22% survive after five years) 72% of the subjects chose the surgery option. However, when the information was framed in a percentage mortality context (10% do not survive the operation and 66% do not survive beyond five years, compared to 0% do not survive radiation treatment and 78% do not survive beyond five years) only 56 % of the subjects chose the surgery option. The mortality frame caused 14 % of the subjects to shift their choice from an "optimal long term survival" choice to an "immediate survival" choice despite the fact that the information presented was identical (Tversky & Kahneman, 1986).

As frequently noted, human reasoning is not a completely rational process; it does not follow the rules of formal logic (Tversky & Kahneman, 1974) and is often influenced by emotions (Frith & Frith, 1979). Stimuli that arouse emotion spontaneously attract attention and can result in an action oriented and unreflective decision-making style (Epstein, 1994). We propose that emotion is one of the key modulatory features of dual-stream processing, biasing decision-making towards the rapid and highly accessible processes of Stream 1 (Figure 4.1a). These features may make Stream 1 processing more advantageous than slower Stream 2 processes in decision-making scenarios where emotion is heightened and swift action is desirable. For example, naturalistic decision-making research has indicated that in jobs where the stakes are high, such as fire-fighting, immediate, intuitive, Stream 1 judgments are superior and, indeed, necessary (Klein, 1999). However, in situations where a more careful consideration of the available evidence is required, the inadequate recruitment of Stream 2 may increase the likelihood of decision-making errors. In this context, the mortality frame in the framing effect example above may represent an emotional bias away from deliberative Stream 2 processes, which would presumably be more adept at identifying the pertinent information relating to improved health prospects in the long-term than the more reactive Stream 1.

Psychosis has been associated with an excessive experience of emotion (Nayani & David, 1996; Freeman, Garety & Kuipers, 2001), with evidence suggesting that people with delusions show a particular bias towards emotional themes congruent with their delusional belief system (Rossell, Shapleske & David, 1998). Compared to non-delusional controls, schizophrenia patients with delusions have also been shown to display an impaired ability to distinguish neutral from aversive events (Jensen et al., 2007), attaching aberrantly increased emotional salience to neutral conditions (Holt et al. 2006). While it has been proposed that the abnormal assignment of emotional salience to neutral stimuli may be a causal factor in the formation of delusions (Kapur, 2003), our dual-stream processing model provides an alternative perspective on the role of emotion in decision-making. In schizophrenia, an aberrantly enhanced emotional response to already salient stimuli may result in a context inappropriate Stream 1 bias, further diminishing the potentially corrective influence of Stream 2 in instances where Stream 1 interpretations are erroneous (Figure 4.1b).

4.2.3 Dual-stream modulation failure summary

In healthy individuals, conflict may serve as a biasing mechanism towards slower, more deliberative Stream 2 processing whereas heightened emotional states may result in a bias towards faster, more reflexive Stream 1 processing. Differential weighting of these modulatory influences between individuals may account for the diversity of opinions expressed when evaluating the same information. Suboptimal functioning of these modulatory influences may contribute to the varying degrees of vulnerability to errors in decision-making that are part of normal human experience. However, severe disruption of the conflict and emotional modulation systems, either individually or in tandem, could lead to a failure in the normal regulation and integration processes between Stream 1 and Stream 2. This pathological schism between Stream 1 and Stream 2 may be the mechanism underlying delusional thinking in schizophrenia, allowing individuals to form and maintain erroneous beliefs without the need to reconcile conflicting evidence.

4.3 Hypothesis validation and future implications

We have proposed a candidate model for a mechanism underlying the formation and maintenance of delusions in schizophrenia. While psychological in flavour, our model functions well within the context of neurophysiological research into the substrates of Stream 1 and Stream 2 reasoning (e.g., Goel & Dolan, 2003a), and both conflict detection and emotion in decision-making (e.g., Greene, Sommerville, Nystrom, Darley & Cohen, 2001; Goel & Dolan, 2003b), giving insight into how failures in these systems may lead to delusional ideation in schizophrenia. The DSMF model may be effectively tested using paradigms that manipulate the agreement between the two streams of processing. In people with schizophrenia, manipulations that induce conflict between the streams should reveal an under-recruitment of areas indicative of reflective, Stream 2 processing, and conflict detection. The use of affective stimuli in such paradigms should activate areas associated with emotion and reflexive Stream 1 processing to a greater extent in people with schizophrenia than in healthy individuals.

DSMF is a general model that utilises the dual-stream framework, and is not proposed as an account for the specific sub-processes that may comprise either stream of reasoning. Further, while DSMF describes general decision-making aberrations that may account for delusion formation and maintenance, and is not a model specific to deductive reasoning, deductive or conditional reasoning paradigms may offer a suitable means by which to initiate experimental investigation of conflict modulation failure and accentuated emotional modulation. For example, in healthy individuals, three-part syllogisms have been successfully employed to investigate the influence of content believability (Stream 1) on judgments of logical validity (Stream 2), for both neutral (Evans, Barston & Pollard, 1983; Goel & Dolan, 2003a) and emotionally salient (Goel & Dolan, 2003b) material, with additional evidence indicating that emotionally salient content or emotional states interfere with deductive reasoning (Blanchette, 2006; Blanchette & Campbell, 2005; Blanchette & Leese, 2011; Blanchette & Richards, 2004; Kemp, Chua, McKenna & David, 1997; Oaksford, Morris, Grainger & Williams, 1996).

As the defining feature of delusions can be considered their maintenance in the face of overwhelming evidence to the contrary, it is appropriate to utilise a paradigm designed to highlight impairments in reasoning when judging the logical validity of belief-inconsistent stimuli. In a previous study using conflict and non-conflict syllogisms to compare the performance of people with schizophrenia to healthy controls, the control group showed the expected decrease in performance for the conflict condition relative to the non-conflict condition (Goel, Bartolo, St Clair & Venneri, 2004). However, while the schizophrenia group performed significantly worse than healthy controls, they were equally impaired for both the conflict and non-conflict conditions, with performance appearing to be at chance levels. It is possible that the three-part syllogisms employed in this study were too demanding for the patient group, resulting in a floor effect and erasing any measurable belief-bias effect. To obviate this possible floor effect, we will design and test a simplified two-part conditional reasoning paradigm. In conjunction with functional imaging techniques, such an approach may be fruitful in providing preliminary validation of our model and the relationship between delusional ideation in schizophrenia and dysfunctions in the operation of dual-stream processing machinery during decision-making.

If validated, the DSMF model could form an important and novel conceptual foundation for more effective non-pharmacological interventions, such as metacognitive training (Moritz & Woodward, 2007). We envision the development of an education strategy or series of exercises designed to endow delusional schizophrenia patients with knowledge of their own reasoning machinery. Such a program would direct attention towards the existence of an underlying processing system that is composed of both fast, associative assessments and slower, deliberative strategies. Augmenting the conscious awareness of conflict between Stream 1 and Stream 2 and the role of emotions in decision-making could lead to the earlier development of insight and enhance adherence to both pharmacological and non-pharmacological treatment programs.

Chapter Five: Behavioural evidence for conflict modulation failure in schizophrenia[4]

5.1 Introduction

In schizophrenia, arbitrary inferences (Kingdon & Turkington, 1991), and a lack of active reality testing (Brett-Jones, Garety & Hemsley, 1987) may result in a circumscribed approach to data gathering conducive to delusional ideation. These tendencies result in a seemingly hasty decision-making style, with judgments made on the basis of little evidence. This is described in the literature as a "jumping-to-conclusions" (JTC) data gathering bias (Garety, Hemsley & Wessely, 1991), and in Chapter Two as a "hypersalience of evidence-hypothesis matches". These approaches provide cognitive accounts for the formation of delusions in schizophrenia. On the other hand, "delusional maintenance models", such as the "bias against disconfirmatory evidence" (BADE) (Woodward, Moritz & Chen, 2006; Woodward, Moritz, Cuttler & Whitman, 2006), highlight the tendency of people with delusions to avoid or discount evidence challenging their beliefs. These tendencies appear very much like an exaggerated form of positive test strategy heuristics prevalent in non-patient controls, such as the confirmation bias (Wason, 1960) and hypothesis preservation (Gorman, 1989). However, in schizophrenia it is more than a simple exaggeration of these mechanisms, it is a pathological resistance to change that no amount of reason or evidence can shift, and represents a fundamental error in decision-making. In Chapter Three this is described as an "evidence integration" deficit.

Cognitive models such as JTC and BADE have made important contributions to our understanding of delusions, showing that these processes apply not only to decisions

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[4] A version of this chapter has been published. Speechley, W., Murray, C., McKay, R., Munz, M., & Ngan, E. (2010). A failure of conflict to modulate dual-stream processing may underlie the formation and maintenance of delusions. *European Psychiatry, 25*(2); 80-6.

relating to the content of a patient's delusional belief system, but that they function in an attenuated form across a range of decision-making scenarios. However, these approaches do not directly address the issue of which core processes are malfunctioning to allow these phenomena to occur in the first place. As Garety and Freeman (1999) have noted, processes such as JTC and BADE, “may serve as maintaining factors or even consequences of current delusional ideation rather than as causes”. Holt et al. (2006) compared JTC in delusional thought to a reliance on “gut” feelings over analytic reasoning, which suggests a potential role for dual-stream information processing theories in developing a mechanistic understanding of this cardinal symptom of schizophrenia.

Dual-stream models of decision-making characterize reasoning as composed of a fast, associative stream that makes automatic, non-deliberative assessments (Stream 1), and a slower, more deliberative stream that requires conscious effort (Stream 2). In Chapter Four we proposed that conflict and emotion are two key dual-stream modulators that may determine the degree of influence each stream exerts over decision-making in a given context, and that aberrations in these modulators may underlie the formation and maintenance of delusions in schizophrenia (Chapter Four: Speechley & Ngan, 2008). The study presented in this chapter is designed to test the conflict modulation arm of the dual-stream modulation failure (DSMF) model of delusions.

When there is a cognitive conflict, as in cases where the two streams suggest different outcomes, this conflict may modulate reasoning towards the deliberative processes of Stream 2. In delusional ideation, convincing counter evidence fails to persuade an individual of the fallaciousness of their views. This fundamental error in decision-making may stem from a failure to detect or adequately respond to the cognitive conflict generated by the divergence of the two streams, resulting in the maladaptive maintenance of Stream 1 processing, and an increased likelihood of erroneous, intuitive judgments.

In the present study we tested the conflict arm of the DSMF model using simple two-part conditional stimuli, e.g., “If some talking creatures are dogs, then some dogs can talk”. By manipulating the agreement between the content believability of a conditional's “then” clause and the logical validity of the whole statement we created both conflict (i.e., beliefs do not match logical validity) and non-conflict (i.e., beliefs match logical validity) conditional stimuli. Our model suggests that the formation and maintenance of delusions in schizophrenia may be related to a failure of conflict to modulate decision-making processes in favour of Stream 2. This could occur either through a failure to detect the conflict, a failure in the modulation process, or both. Regardless of the precise mechanism of conflict modulation failure, the model predicts that, in addition to a generalized performance deficit, patients with schizophrenia will make more errors than healthy controls on the conflict condition compared to the non-conflict condition owing to a greater number of erroneous, belief-biased judgments suggested by associative, Stream 1 processing. The greater success of healthy controls is hypothesized to be due to a greater sensitivity to cognitive conflict, which modulates reasoning towards the deliberative processes of Stream 2.

5.2 Methods

5.2.1 Participants

Twenty-eight participants between the ages of 18 and 55 were recruited. Fourteen were people diagnosed with schizophrenia or schizoaffective disorder and 14 were healthy controls. All had a minimum of eight years of formal education, were proficient in English (receiving at least part of their elementary school education and all subsequent education in English), and had normal or corrected-to-normal visual acuity.

Patients who met DSM-IV-TR (American Psychiatric Association, 2000) diagnostic criteria for schizophrenia, including those with a diagnosis of schizoaffective disorder, were referred to the study team by their treating physician. Diagnoses of schizophrenia or schizoaffective disorder were confirmed by a clinical interview and review of clinical records, conducted by one of the authors (ETN), a licensed psychiatrist. Ten of the 14 patients were stabilized in-patients, nearing discharge, and four were partially remitted outpatients recruited from community mental health teams in Vancouver, British Columbia and outpatient programs at the University of British Columbia Hospital. Patients who met the DSM-IV criteria for substance abuse and dependence, a history of serious head injury, neurological illnesses requiring treatment, or other Axis I diagnoses were excluded from participation in this study. All 14 patients fulfilled the DSM-IV criteria for schizophrenia; one patient also met criteria for schizoaffective disorder. Symptom severity was assessed using the Signs and Symptoms of Psychotic Illness scale (SSPI; Liddle, Ngan, Duffield, Kho & Warren, 2002), a schedule comprising 20 symptom items scored 0–4 according to the severity of the symptom. This scale was administered to all the participants by ETN, a co-developer of the scale, with the mean total symptom score indicating that the patient group was in the moderate range of symptom severity (mean = 12.1, *SD* = 3.9). As we were primarily testing a model for the formation and maintenance of aberrant belief systems, we preferentially selected for schizophrenic patients with aberrant beliefs. Thirteen of the 14 patients endorsed aberrant beliefs; of these 13, eight had definite delusions (SSPI delusions score ≥ 3), and five exhibited unrealistic beliefs bordering on delusions (SSPI delusions score of 1 or 2). All patients were currently receiving oral atypical antipsychotic medication. Nine were receiving one atypical antipsychotic medication (Risperidone, Seroquel or Olanzapine), one was being treated with valproic acid in addition to Risperidone, one received a combination of Risperidone and Seroquel, and the remaining two were treated with Clozapine. The patient also meeting the criteria for schizoaffective disorder was receiving lithium in combination with Olanzapine.

The 14 healthy control participants were recruited through public advertising. In addition to the exclusion criteria for the patients, controls were also excluded if they were currently being treated for a psychiatric condition, had a history of any Axis I diagnosis or had a family history of psychotic illness in a first degree relative.

All participants that took part in the study gave written informed consent after a full explanation of the study and the procedures it involved. All experimental procedures were approved by the University of British Columbia Clinical Research Ethics Board.

5.2.2 Materials

We created a set of 52 two-part conditional statements using subject matter that all participants could be reasonably expected to be familiar with in terms of veracity judgments, e.g., wheels and round, vegetables and nutritious, cigarettes and addictive, and so on. Conditional statements consisted of a single premise (i.e., “If…”) and a single conclusion (i.e., “then…”), with each clause containing a categorical proposition (e.g., all, no, some) or a temporal frequency proposition (e.g., always, sometimes, never). The stimuli were constructed such that the believability of the conclusion either conflicted or agreed with the logical validity of the whole statement. The believability of the conclusion is an automatic judgment indicated by associative, Stream 1 processes, while judging the logical validity of the whole statement requires deliberative, Stream 2 processing. An example of a logically valid stimulus with a believable conclusion is, “If some curious people are children, then some children are curious”. Here, there is no conflict between beliefs and logic, hence, beliefs may facilitate reasoning. An example of a logically valid stimulus with an unbelievable conclusion is, “If some talking creatures are dogs, then some dogs can talk”. Here, beliefs conflict with logic, hence beliefs may interfere with reasoning. Twenty-six of the 52 conditional statements contained belief-logic conflicts, while the remaining 26 were non-conflict stimuli (Appendix III). While the main conditions of interest were conflict and non-conflict, for the purposes of creating a balanced stimulus set an equal number of stimuli were created for all combinations of logical validity and conclusion believability, i.e., 13 of each of the following: valid-believable, valid-unbelievable, invalid-believable, and invalid-unbelievable.

5.2.3 Procedure

Prior to participation in the task, all participants completed an assessment battery consisting of the National Adult Reading Test (NART; Nelson, 1982; Sharpe & O’Carroll, 1991) as a proxy for premorbid IQ, the Ammons Quick Test (QUICK; Ammons & Ammons, 1962) for a proxy assessment of current IQ, and the Hollingshead Two-Factor Index of Social Position (Hollingshead, 1957) as a measure of parental social functioning.

Participants were asked to determine the logical validity of conditional sentences presented on a computer monitor. First, the premise appeared on the screen (i.e, the “if” clause), and participants were instructed to press a button when ready to read the statement’s conclusion (i.e., the “then” clause). The concluding part of the statement then appeared on screen, without removal of the premise, to minimize load on working memory capacity. Once the conditional had been read in its entirety, participants were required to respond “Valid” or “Invalid” via an appropriate button press. To further reduce cognitive demands, the task was self-paced. This procedure was outlined and demonstrated in a training session, in which interactive examples of conditionals were provided and instructions given to emphasize that judgments of validity related to the logical validity of the statements.

The experimental phase consisted of 52 conditional forms. These were presented in four blocks of 13 conditionals, with pseudorandom presentation to ensure approximately equal representation of each conflict and non-conflict conditionals within each block. Performance was recorded as a correct or incorrect assessment of logical validity for each conditional.

5.2.4 Data analysis

A 2×2×2 factorial design was employed. The independent variables were group (healthy controls and people diagnosed with schizophrenia), conflict status (conflict and non-conflict conditionals) and logical validity (logically valid and logically invalid conditionals). An analysis of variance (ANOVA) was conducted using the percentage of correct responses as the dependent variable, with post hoc *t*-tests where appropriate (SPSS 12.0 for Windows, SSPS Inc., Chicago, IL). Between groups analyses of demographic and IQ measures were carried out using two sample *t*-tests, with a Chi-Square goodness-of-fit test for sex. For covariates for which there were significant between groups differences, bivariate Pearson correlation coefficients were calculated to assess the relationship between the covariate and the dependent variable.

5.3 Results

5.3.1 Sociodemographic and psychopathological characteristics

The mean duration of illness for the schizophrenia group was 11 years (SD 7.14 years). The mean total score on the SSPI was 12.1 (SD 3.9), with nine of the 14 participants scoring greater than two on the delusions item, indicating the presence of high levels of delusional ideation in our sample (Table 5.1).

Table 5.1 Socio-demographic and psychopathological information. Values presented are means, with standard deviations in parentheses.

	Schizophrenia (n = 14)	Healthy Control (n = 14)	p-values
Age (years)	36.29 (11.74)	36.14 (12.16)	$p = 0.975$
Gender (Male/Female)	11/3	10/4	$p = 0.676$
Education (years)	12.7 (2.3)	16.2 (3.07)	$p < 0.01$
NART	110.2 (7.2)	117.6 (6.7)	$p < 0.05$
QUICK	98.3 (10.6)	105.4 (11.1)	$p = 0.109$
Length of Illness (years)	11 (7.14)	---	
SSPI Total	12.1 (3.9)	---	

One participant from each group was excluded from between groups NART and QUICK comparisons as they had acquired English proficiency after elementary school. There were no significant between groups differences in age ($t[26] = -0.03$, $p = 0.98$), sex ($\chi 2[1, N = 28] = 0.19$, $p = 0.66$), Hollingshead Index of Social Position ($t[26] = -1.32$, $p = 0.20$), or QUICK scores ($t[24] = 1.67$, $p = 0.11$). There were significant between groups differences in both NART scores ($t[24] = 2.72$, $p < 0.05$) and years of education ($t[26] = 3.42$, $p < 0.01$).

There was no significant correlation between NART scores and the percentage of correct responses for either the schizophrenia group ($r[11] = 0.18$; $p = 0.56$) (Figure 5.1a) or the healthy control group ($r[11] = -0.01$; $p = 0.98$) (Figure 5.1b). The correlation between years of education and percentage correct responses was significant for the schizophrenia group ($r[12] = 0.54$; $p < 0.05$) (Figure 5.2a), but not significant for the healthy control group ($r[12] = -0.05$; $p = 0.87$) (Figure 5.2b).

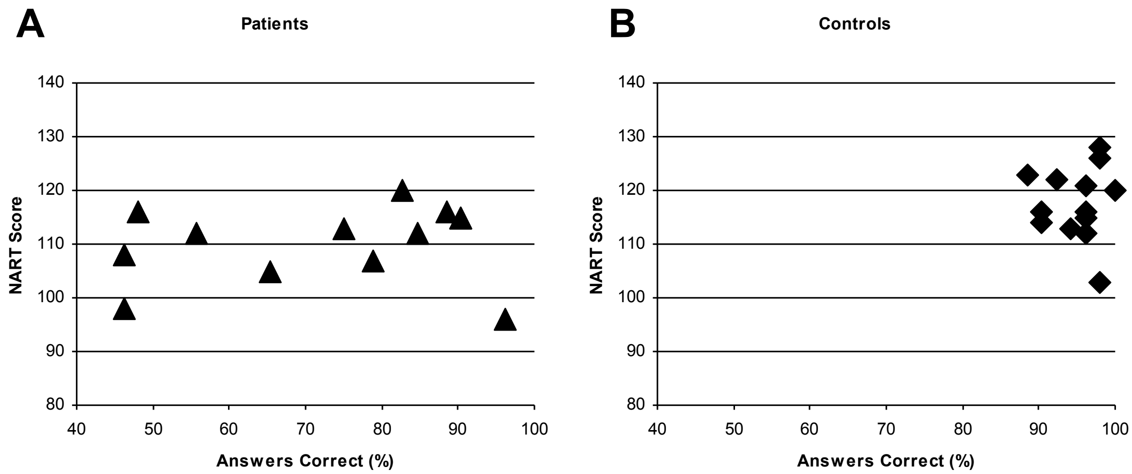

Figure 5.1 Correlation of NART scores with the percentage of correct responses for both the schizophrenia and healthy control groups. The combined groups correlation was significant ($r = 0.40$; $p < 0.05$). Within groups there were no significant correlations between NART scores and percentage of correct responses in either the schizophrenia group ($r = 0.18$; $p = 0.56$) or the control group ($r = -0.01$; $p = 0.98$).

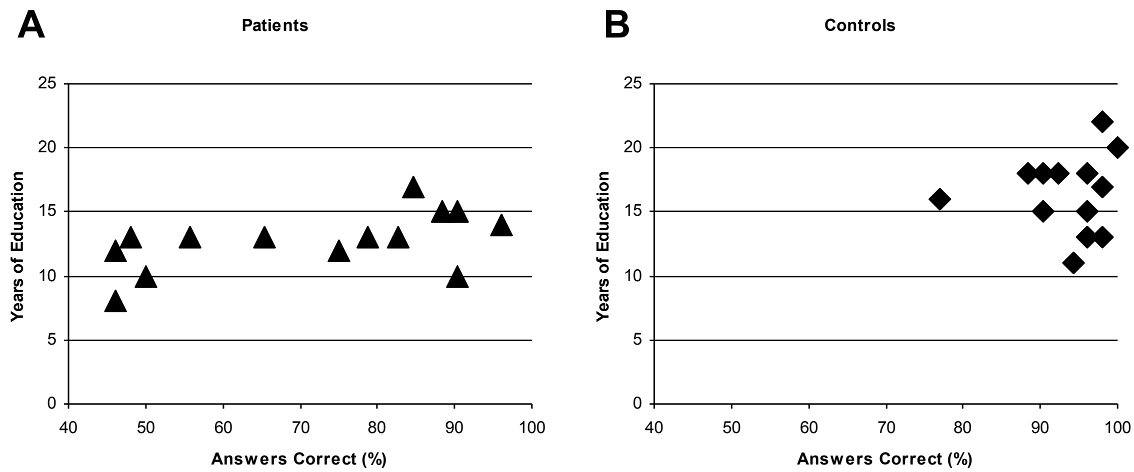

Figure 5.2 Correlation of years of education with percentage of correct responses for both the schizophrenia and healthy control groups. The combined groups correlation was significant ($r = 0.56$; $p < 0.01$). Within groups, the correlation was significant for the schizophrenia group ($r = 0.54$; $p < 0.05$), but not for the control group ($r = -0.05$; $p = 0.87$).

5.3.2 Conditional sentence task performance

The 2×2×2 (group by conflict status by validity) ANOVA revealed a highly significant main effect of group ($F_{1,104}$ = 35.59, $p < 0.001$) and conflict status ($F_{1,104}$ = 7.54, $P < 0.01$), and a significant interaction of group by conflict status ($F_{1,104}$ = 11.09, $p < 0.01$) (Figure 5.3). Post hoc *t*-tests revealed significant differences between the schizophrenia group and control group for both non-conflict (patients = 82.69%, controls = 93.13%; $t[26] = 3.24$, $p < 0.01$) and conflict (patients = 59.89%, controls = 94.23%; $t[26] = 4.17$, $p < 0.001$) conditions. A significant difference between conditions was found for the schizophrenia group (non-conflict = 82.69%, conflict = 59.89%; $t[13] = 3.42$, $p < 0.01$), though there was no significant difference between conditions for the control group.

There was no significant main effect of logical validity ($F_{1,104}$ = 152.68, $p = 0.54$), or significant interaction of group by validity ($F_{1,104}$ = 0.30, $p < 0.58$), conflict status by validity ($F_{1,104}$ = 0.48, $p < 0.49$) or group by conflict status by validity ($F_{1,104}$ = 0.00, $p < 0.97$).

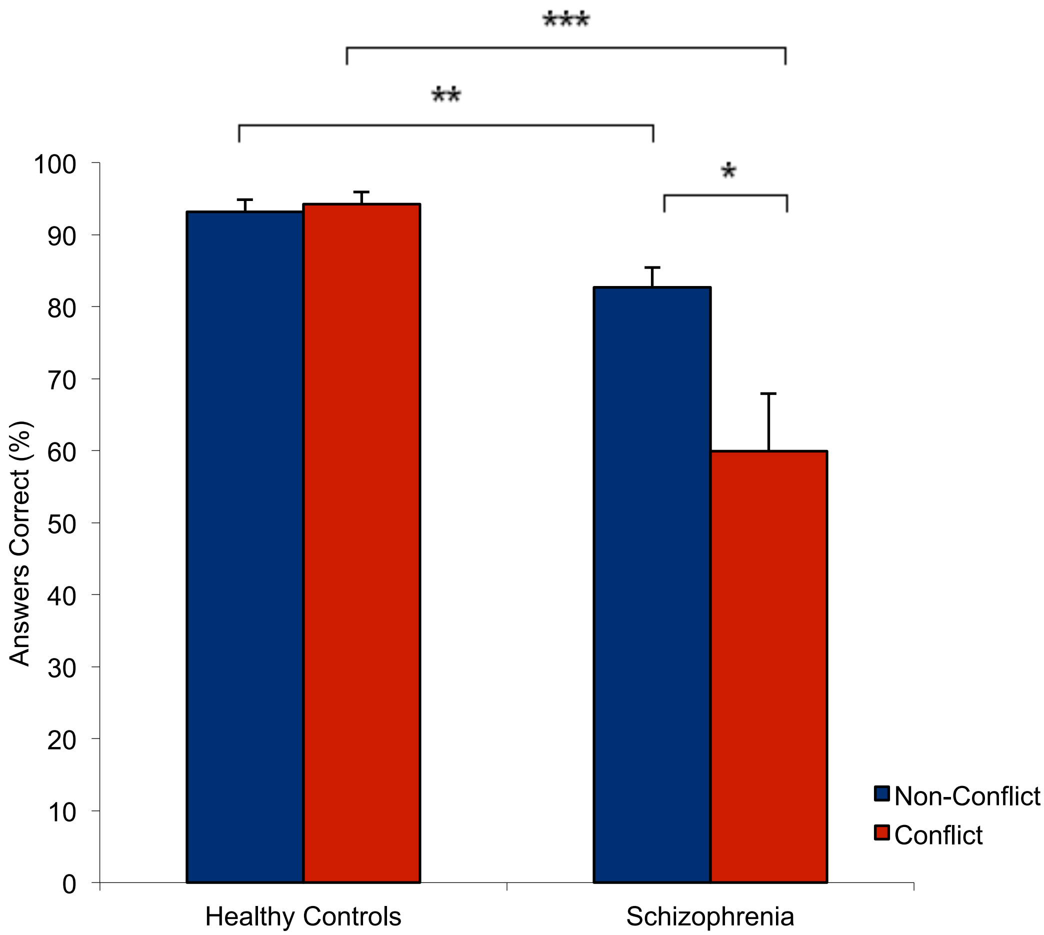

Figure 5.3 The mean percentage of correct responses for the healthy control group (n = 14) and schizophrenia group (n = 14) when assessing the logical validity of conditional statements in which the internal and external validity conflicted (i.e., a conflict between logic and semantic knowledge) or did not conflict (i.e., consensus between both logic and semantic knowledge). The control group performed significantly better than the schizophrenia group on both non-conflict (** = $p < 0.01$) and conflict (*** = $p < 0.001$) conditions. Within groups analyses showed that the schizophrenia group was significantly less accurate at determining the internal validity of conflict conditionals compared to non-conflict (* = $p < 0.05$), while the control group showed no significant difference in performance between conditions (p = 0.658).

5.4 Discussion

The DSMF model proposes two influences on dual-stream reasoning processes that may contribute to the formation and maintenance of delusions in schizophrenia: conflict and emotion (Speechley & Ngan, 2008). This chapter presents a preliminary investigation of, and early support for, the conflict modulation failure arm, which highlights the differing abilities of healthy controls and people diagnosed with schizophrenia to utilize conflict information in decision-making.

Beliefs appear to factor heavily into determinations of logical validity. Specifically, the belief-bias effect shows that irrespective of logical validity, people show a tendency towards endorsement of believable conclusions and rejection of those that are unbelievable. Where both believability and logical validity are consistent there is a facilitatory effect, though when inconsistent, believability can interfere with effective logical evaluation (Evans, Barston & Pollard, 1983). DSMF predicts that the performance deficit resulting from this conflict will be more pronounced for schizophrenia patients with delusions than for non-patient controls. The results support this prediction: in addition to a generalized performance deficit, patients with schizophrenia performed significantly worse when there was a conflict between believability and logical validity, more frequently making erroneous judgments based on the belief-bias influenced initial assessment suggested by associative, Stream 1 processing. Healthy controls performed equally well for both conflict and non-conflict conditions, suggesting a greater ability to reconcile divergent Stream 1 and Stream 2 evaluations. DSMF proposes that conflict modulation increases the likelihood of a judgment in keeping with the available evidence. In patients with schizophrenia, a failure to detect or respond to cognitive conflict may allow erroneous intuitive explanations to coexist with contrary logical explanations of the same event. It is this failure to reconcile or alter beliefs, even when the mounting contradictory evidence is overwhelming, that we believe predisposes towards the formation and maintenance of delusions in schizophrenia.

While the results can be viewed as offering preliminary support for the conflict modulation failure hypothesis, the potential contribution of group differences in demographic variables to the observed results must be considered. There were no group differences in QUICK scores (a proxy measure of current IQ), but the schizophrenia group had significantly lower scores for NART (a proxy measure of premorbid IQ), and significantly fewer years of education than the healthy control group. NART scores did not correlate with performance for either group, but there was a correlation between years of education and performance for the schizophrenia group. The difference in years of education between groups is likely a consequence of illness interrupting education in the schizophrenia group, such that the well-established cognitive deficits associated with schizophrenia may have directly contributed to the differences in years of education. Matching the samples on years of education would require one of the groups to be non-representative (i.e., either highly educated patients or poorly educated controls), and may not even be an appropriate strategy for the schizophrenia group if years of education is a dependent variable for this group. However, in the syllogism literature, years of education and IQ do correlate with performance in healthy controls, and so the difference in years of education cannot be ruled out as a contributing factor to the group difference in performance in the current study, where the schizophrenia group performed worse than healthy controls for both conditions. While years of education may improve general formal logical reasoning skills, it is less clear how years of education would correspond to a specific enhancement in the ability to inhibit belief-biased responding in the conflict condition. Belief-incongruence is considered the source of decreased performance between conditions where syllogisms are formally identical, but populated with content varying in believability. The greater drop in performance for the schizophrenia group for conflict compared to non-conflict conditions suggests a greater susceptibility to the belief-bias effect, in addition to a general performance deficit. The DSMF model suggests the former may be the result of conflict modulation failure.

Potential problems associated with small to medium sample size studies include the increased possibility of Type II errors resulting from a lack of statistical power. With the current sample size we found a highly significant ($p < 0.01$) difference, indicating a large effect size. Another potential issue with small sample sizes is that the groups may not be representative of their respective populations. Because we were testing a model for delusions, we selectively recruited patients who had symptoms associated with delusional thinking. As such, our results may only be applicable to this subgroup of schizophrenia. We cannot comment on the specificity or generalisabilty of our results. Future research incorporating a non-delusional schizophrenia group should be conducted to determine whether or not the findings are specific to the delusional subgroup. Similarly, the inclusion of a non-schizophrenic delusions group will enable us to determine if the results are generalisable to delusional symptoms in other disorders.

An exploratory analysis was performed to determine whether there was any correlation between delusion severity (as measured by item 7 on the SSPI) and performance. This analysis did not reveal a significant relationship between these two measures, but this negative finding should be interpreted with caution as a larger sample size may have more sufficient power to detect a weak relationship. Further, the DSMF model makes no explicit predictions with regards to delusion severity and the degree of conflict modulation failure. While the severity of the CMF effect may predict whether an individual is likely to be delusional, it need not predict the severity of the delusion in the affected individual. In a heterogeneous sample (i.e., a mix of delusional and non-delusional individuals) the two measures will likely be correlated. However, in a homogenous sample (i.e., delusional individuals only) the two measures need not be correlated.

The current stimuli set was successfully constructed with regards to placing the believability of the conclusion in agreement or conflict with the logical validity of the whole two-part conditional statement. However, some of the stimuli used in the current study may potentially have introduced a group by condition by general knowledge application interaction. For example, “If tires are always made of glass, then some tires are made of rubber”, and “If all cars run on gasoline, then some cars run on water”, require the knowledge that glass is not rubber, and gasoline is not water. While it is unlikely that there are between group differences with regards to having this knowledge, there may be group differences in the ability to effectively apply this knowledge within the context of the task. The study presented in Chapter Six will remove this potential confound by utilising only pairs of stimuli repeated in both the premise and the conclusion.

5.5 Conclusion

The current results provide encouraging preliminary support for the conflict modulation failure arm of the DSMF model of delusions in schizophrenia (Speechley & Ngan, 2008), and suggest the viability of the two-part conditional reasoning paradigm for further investigation of the model. In Chapter Six, further validation of the conflict modulation failure effect will be sought utilising functional magnetic resonance imaging to identify its potential neurophysiological correlates. The following chapter will also address the full DSMF model by including affective stimuli to investigate the potential role of emotional salience in aberrantly modulating decision-making away from Stream 2 and towards Stream 1 in schizophrenia.

Chapter Six: An fMRI investigation of the dual-stream modulation failure model of delusions in schizophrenia[5]

6.1 Introduction

The Diagnostic and Statistical Manual of Mental Disorders (DSM-IV TR; American Psychiatric Association, 2000) defines delusions as false beliefs based on incorrect inferences about external reality that are firmly sustained despite what almost everybody else believes and despite what constitutes incontrovertible and obvious proof or evidence to the contrary. This definition continues to generate debate concerning the necessity and sufficiency of its component parts to the extent that David (1999) has gone as far as to suggest that the generation of an adequate definition of delusions may not even be possible. However, despite the difficulty in pinning down an acceptable definition, it remains uncontroversial that delusions are one of the cardinal, and most debilitating symptoms of schizophrenia. While there have been improvements in treatment compliance due to the improved tolerability of atypical neuroleptics, medications remain partially effective for some and completely ineffective for others. Further improvements in the management of schizophrenia will require further advances in our understanding of the neuropathophysiology of psychosis. The rapid development of neuroimaging technologies and new models of human decision-making across the last decade have provided an opportunity to improve our knowledge of the cognitive and neuropathophysiological basis for psychosis in general and delusions in particular.

[5] A version of this chapter is in preparation for submission. Speechley, W., Woodward, T. S., & Ngan, E. (in preparation). The neural correlates of Dual-Stream Modulation Failure in schizophrenia.

The dual-stream modulation failure (DSMF) model (Speechley & Ngan, 2008; Speechley et al., 2010) is a general cognitive model that suggests mechanisms for the both the formation and maintenance of delusions, and has the potential to account for the expression of previously identified cognitive biases, such as the jumping-to-conclusions bias (JTC; Garety, Hemsley & Wessely, 2001; Moritz & Woodward, 2005; Speechley, Whitman & Woodward, 2010), the hypersalience of evidence-hypothesis matches (Speechley, Whitman & Woodward, 2010), and the bias against disconfirmatory evidence (BADE; Woodward, Moritz & Chen, 2006; Woodward, Moritz, Cuttler & Whitman, 2006; Speechley et al., in press). This model suggests that the degree to which an individual utilises reflexive (Stream 1) versus reflective (Stream 2) decision-making processes is determined by two modulating factors: conflict and emotional salience (Speechley & Ngan, 2008). Specifically, a processing conflict may generate a sense of dissonance that may modulate decision-making towards Stream 2, initiating a more thorough consideration of the available evidence, while emotional salience may tip the balance towards the more reflexive, Stream 1 mode of processing. Severe aberrations of the modulators, either individually or in tandem, may underlie the formation and maintenance of delusions in schizophrenia. In the DSMF model, these two cognitive deficits are described as conflict modulation failure (CMF) and accentuated emotional modulation (AEM).

In schizophrenia, CMF represents a relative failure of conflict to modulate decision-making towards Stream 2, decreasing the impact of contradictory evidence on reasoning and increasing the likelihood that erroneous, intuitive interpretations will endure, uncorrected. Behavioural data presented in Chapter Five provided preliminary support for the CMF arm of the DSMF model. Participants completed a simple two-part conditional reasoning paradigm that placed content believability (a Stream 1 judgment) in agreement or conflict with logical validity (a Stream 2 judgment). Compared to healthy controls, the schizophrenia group showed a significantly greater decrease in performance for the conflict condition compared to the non-conflict condition. In the context of the DSMF model, the greater number of erroneous, believability lead judgments made by the schizophrenia group was interpreted as being the result of inadequate modulation towards deliberative, Stream 2 processing when confronted with cognitive conflict (Speechley, Murray, McKay, Munz & Ngan, 2010).

In addition to further exploration of the CMF arm of the model, this chapter also considers the remaining arm of the DSMF model, which addresses the influence of affect on reasoning. Real-world decision-making is substantially influenced by emotion, which may modulate decision-making towards more reflexive, intuitive modes of processing, and away from “cold”, logical reasoning. This may be advantageous in situations where emotion is heightened and quick, decisive decisions are necessary (e.g., fight or flight scenarios), but where deliberation may be more advantageous, emotionally biased Stream 1 responses may result in suboptimal decisions. A healthy person may exhibit diminished logical reasoning when influenced by emotion, such as an inability to see anything but faults in a person that is disliked or a tendency to see no flaws in superficially supported, but strongly held personal opinions. Bleuler (1911) saw such “healthy” behaviours as being only quantitatively different from delusions, describing a breakdown in the balance between affect and logic that allows emotions to direct reasoning in delusions.

Affect has had a central position in theories of delusions for nearly a century, with a number of early theorists identifying an exaggeration of affect as a key cause of delusional thinking (review: Winters & Neale, 1983). More recently, Kapur’s “aberrant salience” model (2003) suggested that neutral stimuli can become imbued with emotional salience in psychosis, with dysregulated dopamine transmission in schizophrenia potentially resulting in context inappropriate salience attributions, exaggerating the importance of percepts. However, this contrasts with research noting that the salient themes that dominate healthy mental life (e.g., religion, death, freedom, etc) also form the basis of most delusions (e.g., Garety, Hemsley & Wessely, 2001). As Kraepelin (1921) noted, "…the various directions, which the delusions take in paranoia, correspond in general to the common fears and hopes of the normal human being. They, therefore, appear in a certain manner as the morbidly transformed expression of the natural emotions of the human heart." Anxiety, depression and irritability typically precede the manifestation of positive symptoms, and have been shown to be predictive of positive symptom formation (Krabbendam, Janssen, Bijl, Vollerburgh & van Os, 2002). Psychosis itself has also been associated with an excessive experience of emotion (Nayani & David, 1996; Freeman, Garety & Kuipers, 2001), with evidence suggesting that people with delusions show a particular bias towards emotional themes congruent with their delusional belief system (Rossell, Shapleske & David, 1998). What is important to an individual may become disconnected from logical processes and take on a delusional character. Consistent with this research, DSMF indicates that the influence of emotion on reasoning may be abnormally accentuated in schizophrenia, such that, for emotionally salient information, AEM may aberrantly tip the balance of reasoning towards Stream 1 processing, and away from Stream 2. This may diminish the potentially corrective influence of Stream 2 in instances where emotionally biased Stream 1 interpretations are erroneous.

The current study was designed to determine the neurophysiological correlates of the previous behavioural CMF results by using functional magnetic resonance imaging (fMRI) in conjunction with the two-part conditional reasoning paradigm. In this study, the stimuli will include both neutral and emotionally salient content to assess whether there is any additional impact of emotional salience on dual-stream processing suggestive of emotional modulation for healthy controls and AEM for people diagnosed with schizophrenia.

Predicted correlates of conflict modulation failure include regions involved in conflict detection and deliberative, logical reasoning or conflict resolution. The deliberative functions of Stream 2 are likely to employ lateral and dorsolateral frontal cortex regions. These regions are consistently implicated in a variety of executive reasoning tasks, including the Wisconsin Card Sorting Test (Drewe, 1974; Konishi et al., 1999a; Konishi et al., 1999b; Stuss et al., 2000; Lie, Specht, Marshall & Fink, 2006) and the Tower of London test (Shallice, 1988; Rowe, Owen, Johnsrude & Passingham, 2001), and in both deductive and inductive reasoning tasks (Parsons & Osherson, 2001; Goel, Buchel, Frith & Dolan, 2000; Goel & Dolan 2003a; Goel & Dolan, 2004). The network of areas activated in studies utilising both inductive and deductive reasoning also typically includes the parietal cortex (Goel, Gold, Kapur & Houle, 1997, 1998; Osherson et al., 1998; Goel, Buchel, Frith & Dolan, 2000; Goel & Dolan, 2003a; Goel & Dolan, 2004; Noveck, Goel & Smith, 2004). While involved in deliberative reasoning more generally, the parietal cortex has also been identified as particularly associated with reasoning trials using either belief-neutral or abstract content (Goel, Buchel, Frith & Dolan, 2000; Goel & Dolan, 2003a; Noveck, Goel & Smith, 2004), suggesting its role in processing using formal logical structures independent of meaningful content.

The conflict detection and modulatory functions that are proposed to lead to engagement of Stream 2 likely involve the dorsal anterior cingulate cortex (dACC). Past research has shows that the dACC activates in the presence of cognitive conflict, for example, when encountering incongruent stimuli in the Stroop Task (Pardo, Pardo, Janer & Raichle, 1990; Carter, Mintun, Nichols & Cohen, 1997; Ruff CC, Woodward, Laurens, Liddle, 2001) and the Go/No-Go Task (Casey et al., 1997). The conflict modulation arm of the dual-stream modulation model suggests that the presence of cognitive conflict leads to activation of neural regions responsible for mediating a bias towards Stream 2 processing, increasing the likelihood of a response in keeping with the available evidence. This proposal is consistent with a number of theories of dACC function, all of which suggest that, in the presence of cognitive conflict, the dACC signals to other cortical regions that adjustments are needed in order to optimize performance (Botvinick, Braver, Barch, Carter & Cohen, 2001; Luks, Simpson, Feiwell & Miller, 2002; Gehring & Taylor, 2004; Hayden & Platt, 2006; Behrens, Woolrich, Walton & Rushworth, 2007; Woodward, Metzak, Meier & Holroyd, 2008). These other neural networks work to make adjustments that will resolve this cognitive conflict, assigning attention to optimize performance. In accordance with this account, dACC activation is highest when an incongruent trial follows a congruent (Botvinick, Nystrom, Fissell, Carter & Cohen, 1999; Kerns et al., 2004), and dACC activation for an incongruent trial predicts increased frontal activation in subsequent trials (Kerns et al., 2004).

Two separate pathways have been identified as responsive to emotionally arousing stimuli: a basolateral amygdala–orbitofrontal cortex (OFC)–rostral insula pathway, and a ventromedial prefrontal cortex (VMPFC)–subgenual ACC–amygdala pathway (reviews: Carmichael & Price, 1996; Elliott, Dolan & Frith, 2000; Ongur & Price, 2000). Inclusion of the OFC and VMPFC in these emotional processing pathways is notable given the possible association of this area of the brain with Stream 1 processing. Stream 1 is an automatic, intuitive form of processing that draws upon past experiences and associations. Moscovitch

& Winocur (2002) describe intuition as an experience of 'felt-rightness', suggesting that in conditions of uncertainty it is the VMPFC that signals the felt-rightness of an assessment before any further processing or verification is carried out by the DLPFC. The "belief-bias" effect that leads to erroneous answers for conflict stimuli in conditional reasoning paradigms can be understood as the result of deliberative Stream 2 decisions that are unduly influenced by default impressions generated by Stream 1. A failure to inhibit belief-biased responding when judging the logical validity of neutral content syllogisms has been associated with increased VMPFC activity (Goel & Dolan, 2003a). Further, when emotionally salient syllogism content was compared to neutral content, VMPFC activity was relatively enhanced, and lateral and dorsolateral PFC (L/DLPFC) activity relatively suppressed, with the reverse pattern of enhancement and suppression for neutral content trials (Goel & Dolan, 2003b). This is consistent with emotional modulation in the DSMF model, which suggests that emotional salience is associated with a decrease in Stream 2 processing and/or an increase in Stream 1 processing.

DSMF proposes that the formation and maintenance of delusions in schizophrenia may be associated with:

1. A failure of cognitive conflict to modulate reasoning towards deliberative Stream 2, and away from intuitive Stream 1, and/or
2. Emotional salience exerting an aberrantly powerful bias away from Stream 2 processing, and towards Stream 1.

While our two-part conditional reasoning paradigm is explicitly designed to engage automatic, believability mediated processing (Stream 1) to the detriment of deliberative processes (Stream 2), the task itself is decidedly Stream 2 in nature. Stream 1 may exert an influence over the deliberative Stream 2 processes essential for appropriate engagement with the task, but it is not expected that task manipulations will result in participants disengaging with the task and attempting to solve the task using Stream 1 process alone. For these reasons we will consider the DSMF fMRI predictions in terms of modulation towards and away from deliberative Stream 2, rather than towards and away from associative Stream 1.

Given the association of dACC and frontal cortex regions with the detection and resolution of cognitive conflict, greater dACC and frontal activation is anticipated for the conflict condition than for the non-conflict condition in both patients and controls. CMF predicts that the schizophrenia group will show a smaller increase in activation in dACC and frontal cortex regions for the conflict condition than healthy controls. VMPFC has been associated with both Stream 1-like processing and affective processing. However, the literature also suggests an anti-correlation between L/DLPFC and VMPFC activity (Gunsard & Raichle, 2001; Raichle et al., 2001; Goel & Dolan, 2003b), with cognitive demands increasing L/DLPFC and decreasing VMPFC, and affect decreasing L/DLPFC and increasing VMPFC (Simpson et al., 2001; Ochsner & Gross, 2005; Erk, Kleczar & Walter, 2007). As our two-part conditional paradigm is a “Stream 2 task”, it may be most appropriate to consider the influence of emotional modulation on L/DLPFC activity. This approach suggests decreased L/DLPFC activity for emotionally salient stimuli compared to neutral, owing to emotional modulation away from Stream 2 processing. AEM suggests that this difference will be greater for the schizophrenia group than the healthy control group.

6.2 Methods

6.2.1 Participants

Twenty-one participants with schizophrenia and 21 healthy control participants were recruited. All were right-handed, between 20 and 58 years of age, were proficient in English (receiving at least part of their elementary school education and all subsequent education in English), and had normal or corrected-to-normal visual acuity.

Participants in the schizophrenia group were recruited from inpatient psychiatric units at Vancouver General Hospital and the University of British Columbia (UBC) Hospital, affiliated outpatient psychiatric programs, and by advertisement in local newspapers. Patients were diagnosed with schizophrenia or schizoaffective disorder by their hospital or community treating psychiatrist. This diagnosis was confirmed in a separate diagnostic interview conducted by the investigation psychiatrist (ETN). All patients fulfilled the DSM-IV criteria for schizophrenia, though three patients also met the criteria for schizoaffective disorder. Those who met the DSM-IV criteria for substance abuse and dependence, or had a history of serious head injury were excluded from participation in this study. Symptom severity was assessed using the Signs and Symptoms of Psychotic Illness scale (SSPI; Liddle, Ngan, Duffield, Kho & Warren, 2002), a symptom scale comprising 20 items scored 0–4 according to severity. This scale was administered to all the participants by ETN, a co-developer of the scale, with the mean total symptom score indicating that the patient group was in the moderate range of symptom severity (mean = 9.86, SD = 5.71). As this study was designed to test a model for the formation and maintenance of aberrant belief systems, we preferentially selected for schizophrenia patients with aberrant beliefs. All patients were taking a stable dose of neuroleptic medication, defined as no changes in regular dosages of medication and no requirement for as needed (prn) medications in the four weeks prior to participation in this study. Twelve participants in this group were receiving one atypical antipsychotic medication (clozaril, olanzapine, risperidone or quetiapine), one was receiving one typical antipsychotic medication (pipotiazine), and the remaining eight were receiving one of the following combinations of medications: clozaril and lamotrigine; clozaril and valproic acid; risperidone and valproic acid; risperidone and quetiapine; quetiapine, ziprasidone and methotrimeprazine; olanzapine, quetiapine and divalproex sodium; flupentixol and lithium carbonate; loxapine and aripiprazole.

Healthy control participants were recruited through public advertising. In addition to the exclusion criteria for the patients, controls were also excluded if they were currently being treated for a psychiatric condition, had a history of any Axis I diagnosis or had a family history of psychotic illness in a first degree relative. All participants that took part in the study gave written informed consent after a full explanation of the study and the procedures it involved. All experimental procedures were approved by the University of British Columbia Clinical Research Ethics Board.

6.2.2 Materials

Conditional statements were constructed using a single premise (i.e., “If. . .”) and a single conclusion (i.e., “then. . .”), with each clause containing a categorical proposition (i.e., all, no, some, some not), e.g., “If no A’s are B’s, then all B’s are A’s”. Both internal and external validity were considered when constructing the conditional statements. Internal validity refers to the logical validity of the whole statement; a deliberative, Stream 2 assessment of whether or not the conclusion logically follows the premise. Internal validity is determined by the specific pairing of categorical propositions used, not the subject matter. So, “If no A’s are B’s, then all B’s are A’s”, is logically invalid regardless of whether the subject pair A and B refers to bank tellers and women (“If no bank tellers are women, then all women are bank tellers”) or criminals and rapists (“If no criminals are rapists, then all rapists are criminals”) as it is constructed using the categorical proposition pair, “no…all”. External validity is the logical validity of the conclusion independent from the premise. It can be considered the “believability” of the conclusion; an associative, Stream 1 assessment of the consistency between the conclusion and the participant’s semantic knowledge base. External validity is a function of both the subject and its categorical proposition, e.g. “all women are bank tellers”, is externally invalid, while, “all rapists are criminals”, is externally valid. The dissociation between internal validity and external validity allows for the creation of conditional statements where internal validity and external validity either conflict (beliefs do not match logical validity) or agree (i.e., beliefs match logical validity).

Forty neutral stimuli were created from 20 subject pairs that all participants could be reasonably expected to be familiar with in terms of veracity judgments, e.g., wheels and round, vegetables and nutritious, cigarettes and addictive, and so on. Each item was used to create both a conflict and a non-conflict statement.

An emotionally salient stimuli set was selected using a pilot questionnaire of 80 emotionally salient statements that was given to 15 healthy control participants. The statements were of a form that could be readily translated into two-part conditional sentences (e.g., “Rapists are criminals” could become “If no criminals are rapists, then no rapists are criminals”). Participants rated each statement for “valence” (a seven point scale ranging from “Strongly Disagree” to “Strongly Agree”) and “arousal” (a five point scale ranging from “low” to “high” arousal). Research using the Self-Assessment Manikin (Lang, 1980; Hodes, Cook & Lang, 1985; Bradley & Lang, 1994) has shown that the most emotionally salient stimuli are those that are rated at the extremes for both valence and arousal, with increases in ratings on one scale generally corresponding to increases in the ratings for the other. As such, we calculated emotional salience by summing the ratings for valence and arousal, with the most salient items being considered those with the highest summed score. The 20 most emotionally salient items across all participants were selected to create 40 stimuli, with each item being used to create a conflict and a non-conflict statement.

6.2.3 Procedure

Prior to participation in the task, all participants were screened for safety for high-field MRI in accordance with the guidelines of the UBC High Field MRI Centre, provided informed consent, and completed an assessment battery consisting of the National Adult Reading Test (NART) (Nelson, 1982) as a proxy for premorbid IQ, and the Ammons Quick Test (QUICK; Ammons & Ammons, 1962) as a proxy for current IQ. A training session was given on a laptop computer to familiarise participants with the conditional reasoning task and its timing. Instructions were given making it clear that determinations of logical validity related to the internal validity of the statements. When it was clear that the task was understood (operationalised as six of eight neutral exemplars being answered correctly), the experimental phase was initiated.

Participants underwent fMRI (3.0 Tesla Philips Achieva) scanning while determining the logical validity of conditional sentences constructed as described in detail above. Responses were given by pressing one of two buttons to indicate whether conditional sentences were logically valid or logically invalid. Each trial began with a three second presentation of the “If” clause, followed by presentation of the whole “If…then” statement for a maximum of nine seconds further. When a response was given, via button press, the statement was replaced with a crosshair for three, four or five seconds. Trials were separated by crosshair presentation regardless of whether a response was given or not.

The study comprised four runs of 20 conditional sentences for a total of 80 conditional sentences. Forty were neutral stimuli and 40 emotionally salient. Of each 40, 20 were conflict stimuli and 20 were non-conflict stimuli. Each of the four runs was balanced for conflict status, salience and internal validity. Five null periods of 15, 16 or 17 seconds occurred randomly across each run. The inclusion of null events provides trial-free periods, allowing baseline levels of activation to be attained (Friston, Zarahn, Josephs, Henson & Dale, 1999).

6.2.4 Image acquisition and processing

Echo-planar images were collected on a Philips Achieva 3.0-T scanner, equipped with a SENSE coil. Conventional spin-echo T1-weighted sagittal localisers were used to view head position and to graphically prescribe the functional image volumes. Functional image volumes sensitive to the blood-oxygen-level-dependent (BOLD) contrast signal were collected with a gradient echo sequence (TR/TE 2000/30 ms, 90º flip angle, FOV 216 mm x 143 mm x 240 mm (AP, FH, RL), 3.00 mm slice thickness, 1 mm slice gap, and 36 axial slices). Functional images were reconstructed offline. Statistical Parametric Mapping software (SPM5, Wellcome Institute of Cognitive Neurology) was used for image reorientation, realignment, normalization into Montreal Neurological Institute space, and smoothing with a Gaussian kernel (8mm full width at half maximum) to compensate for inter-participant anatomical differences and optimize the signal-to-noise ratio.

6.2.5 Data analysis

Between groups analyses of demographic and IQ measures were carried out using two sample t-tests, with a Chi-Square goodness-of-fit test for sex.

Behavioural data (response accuracy) was analysed using a 2x2x2 analyses of variance (ANOVA) with post-hoc t-tests as appropriate (SPSS 12.0 for Windows, SSPS Inc., Chicago, IL). A trial was recorded as an error if either an incorrect response was given or no response was given before the beginning of the next trial. The independent variables were group (healthy controls and participants diagnosed with schizophrenia), conflict status (conflict and non-conflict conditionals), and salience (neutral and emotionally salient). The dependent variable was response accuracy (percentage of correct responses). Additional t-tests were carried out to determine whether the difference between conditions (conflict minus non-conflict) was significantly different between groups for both neutral and emotionally salient stimuli. Statistical tests for behavioural and functional imaging data were one-tailed, reflecting the directional nature of our hypotheses.

fMRI data analysis comprised three stages: **1.** The task related BOLD response was estimated using a set of ten finite impulse response (FIR) functions (Henson, Rugg & Friston, 2001; Manoach, Greve, Lindgren & Dale, 2003) corresponding to the ten repetition times (20 seconds) immediately following the presentation of each "If…" statement. FIR models make no *a priori* assumptions with regards to the shape and time course of haemodynamic response functions, and thus, avoid errors associated with ill-fitting canonical models (Handwerker, Ollinger & D'Esposito, 2004). **2.** The beta estimates for the FIR models were brought forward for a second level analysis to identify the networks of brain regions that showed significant activity during task performance ($t = 7.94$, $p = 0.00001$, corrected for multiple comparisons). To avoid a group or condition bias, this analysis was performed on all participants for all conditions combined. If we had, for example, utilised only the healthy control group to identify the regions involved task performance, this may have generated a different map of significantly activated regions than would have been identified using the schizophrenia group alone, biasing the results in favour of the control group. **3.** The beta estimates for each FIR function for each voxel within the identified network were extracted for each participant for each stimulus type. The mean beta estimates for time bins four to six were calculated and used as dependent variables in 2x2x2 (group by conflict status by salience) ANOVAs, with post-hoc t-tests as appropriate. Time bins four through six were chosen to maximize the signal-to-noise ratio as a review of the haemodynamic response indicated that the peak BOLD response occurred during this period for both groups and both conditions (Figure 6.1).

To test the primary hypothesis that healthy controls would show a greater increase in activity than the schizophrenia group for the conflict condition compared to the non-conflict condition, the mean beta estimate for the non-conflict condition was subtracted from the mean beta estimate for the conflict condition (i.e., conflict minus non-conflict) for each subject in each group and used as the dependent variable for independent samples t-tests. To test the hypothesis that the schizophrenia group would show bigger decreases in activity between emotionally salient and neutral stimuli than healthy controls, the mean beta estimate for the neutral condition was subtracted from the mean beta estimate for the emotionally salient condition (i.e., emotionally salient minus neutral) for each subject in each group and used as the dependent variable for independent samples t-tests.

Bivariate Pearson correlation coefficients were calculated using performance on the conflict condition and mean beta values for the conflict condition to test whether there was a positive correlation between success on the conflict condition and amount of activity for the whole task activation network.

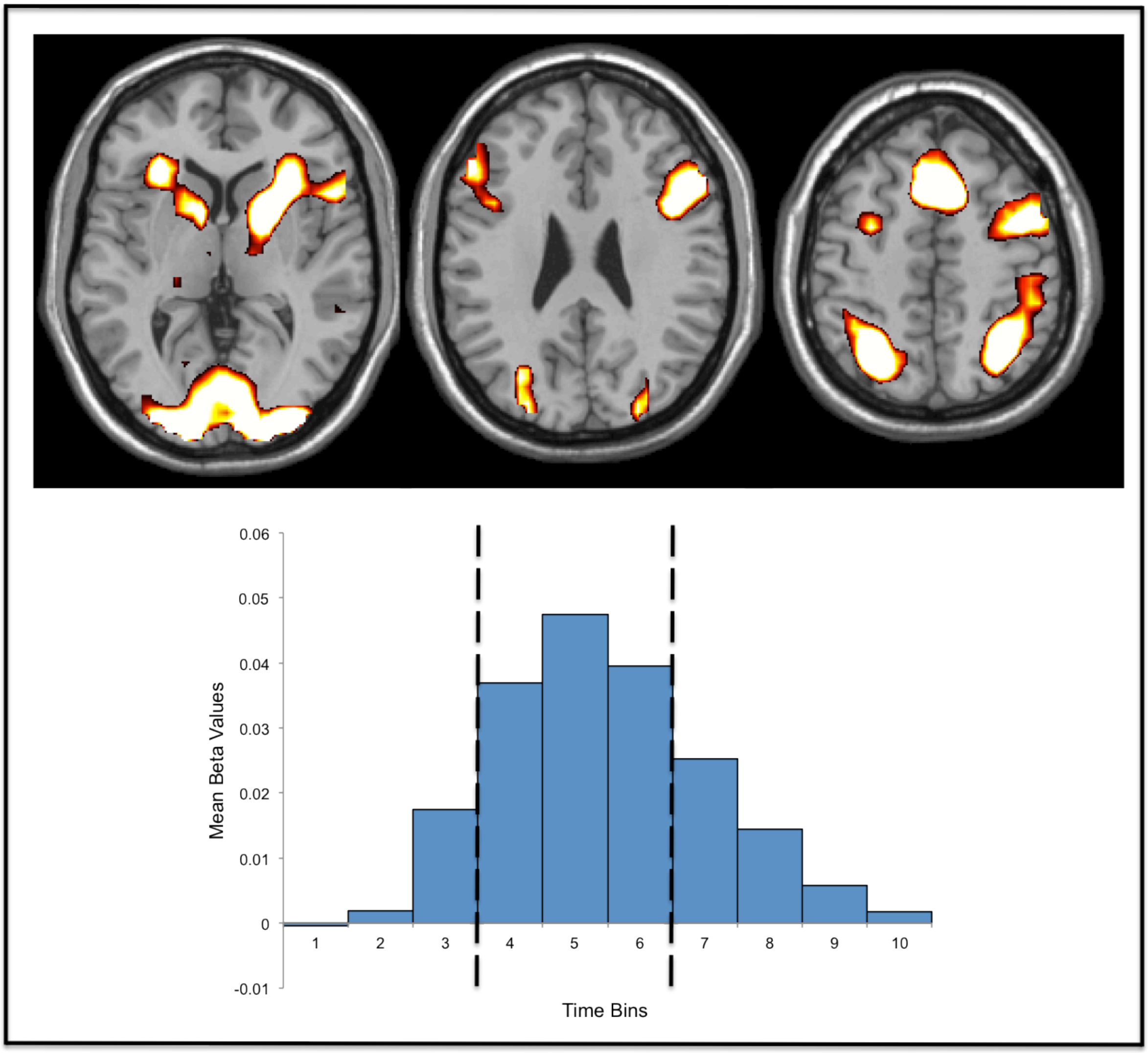

Figure 6.1 *Above:* Regions of activation for the mask of task related activity. *Below:* Finite Impulse Response (FIR) basis set (10 time bins) for the mask of task related activity, indicating the peak hemodynamic response occurring during time bin five, and the three time bins used for beta estimate extraction (bins four through six). Both activations and the FIR basis set present data for both groups.

6.3 Results

6.3.1 Sociodemographic and psychopathological characteristics (Table 6.1)

The mean duration of illness for the patient group was 15.67 years (SD 10.89 years). The mean total score on the SSPI was 9.86 (SD 5.71). Sixteen of the 21 patients endorsed aberrant beliefs; of these 16, five had severe delusions (SSPI delusions score = 4), six had definite delusions (SSPI delusions score = 3), and five exhibited unrealistic beliefs bordering on delusions (SSPI delusions score of 1 or 2).

There were no significant between groups differences in age (t[40] = -0.238, p = 0.81), sex (χ_2 [1,N = 40] = 0.00, p = 1.00), QUICK scores (t[40] = 1.109, p = 0.27) or NART scores (t[40] = 0.09, p = 0.93). There was a significant between groups difference for years of education (t[40] = 1.996, p = 0.05). However, there were no significant correlations between years of education and performance (percentage answered correctly) for either group (Controls: r[21] = -0.093, p = 0.688; Sz: r[21] = 0.133, p = 0.566).

Table 6.1 Sociodemographic and psychopathological group characteristics. Mean values, with standard deviations in parentheses are presented.

	Healthy Controls (n=21)	Schizophrenia (n=21)	t-value	*p*-value
Age (Years)	33.86 (10.76)	34.67 (11.25)	-0.238	0.813
Sex (M:F)	14:7	14:7	0.000	1.000
Education (Years)	15.24 (2.23)	13.76 (2.55)	1.996	0.053
NART (IQ)	118.86 (4.88)	119 (5.34)	-0.090	0.928
QUICK (IQ)	109.9 (10.47)	105.6 (14.2)	1.109	0.274
Illness Duration (Years)	n/a	15.67 (10.89)		
SSPI (Delusions)	n/a	2.14 (1.56)		
SSPI (Total)	n/a	9.86 (5.71)		

6.3.2 Behavioural results

6.3.2.1 Main effects and interactions

The mean group performance (percentage of conditionals answered correctly) for all conditions is shown in Figure 6.2, and Table 6.2. The 2x2x2 (group by salience by conflict status) ANOVA indicated highly significant main effects of group ($F_{1,160} = 32.25$, $p < 0.001$) and conflict status ($F_{1,160} = 32.25$, $p < 0.001$), with a significant interaction of group by conflict status ($F_{1,160} = 7.17$, $p < 0.01$). There was no significant main effect of salience ($p = 0.21$) and no significant interactions of group by salience ($p = 0.75$), salience by conflict status ($p = 0.88$) or group by salience by conflict status ($p = 0.66$).

6.3.2.2 Between groups t-tests

Mean values for all conditions are presented in Table 6.2. Post-hoc t-tests indicated that the control group performed significantly better than the schizophrenia group for all conditions: Neutral (t[20] = 3.54, $p < 0.001$), Affective (t[20] = 3.45, $p < 0.001$), Non-Conflict (t[20] = 2.96, $p < 0.005$), Conflict (t[20] = 3.33, $p < 0.001$), Neutral Non-Conflict (t[20] = 2.39, $p < 0.05$), Neutral Conflict (t[20] = 3.38, $p < 0.01$), Affective Non-Conflict (t[20] = 3.09, $p < 0.01$) and Affective Conflict (t[20] = 3.04, $p < 0.01$).

T-tests comparing the difference between conditions (Non-Conflict minus Conflict) indicated that the schizophrenia group had a significantly greater decrease in performance than the healthy control group for both Neutral (Controls = 5.24% (SD = 6.61), Sz = 17.86% (SD = 19.97); t[20] = -2.75, $p < 0.01$) and Affective (Controls = 7.62% (SD = 10.08), Sz = 16.67% (SD = 19.45); t[20] = -1.89, $p < 0.05$) conditionals.

An additional between groups analysis was conducted using the SSPI delusions item to separate out a severely delusional schizophrenia group (*n* = 5) from the rest of the schizophrenia group (n = 16) (delusions item = 4, and < 4, respectively). However, no comparisons between these two groups were significant.

Table 6.2 Summary of between group behavioural data and t-tests. Mean values, with standard deviations in parentheses are presented.

	Healthy Controls	Schizophrenia	t-value	*p*-value
Neutral	94.76 (3.78)	83.93 (13.5)	3.54	$p < 0.001$
Affective	92.86 (5.08)	80.71 (15.31)	3.45	$p < 0.001$
Conflict	90.6 (6.56)	73.69 (33.33)	3.33	$p < 0.001$
Non-Conflict	97.02 (3.32)	90.95 (8.78)	2.96	$p < 0.005$
Neutral-Conflict	92.14 (5.82)	75.00 (22.47)	3.38	$p < 0.01$
Neutral Non-Conflict	97.38 (4.07)	92.86 (7.68)	2.39	$p < 0.05$
Affective Conflict	89.05 (9.44)	72.38 (23.32)	3.04	$p < 0.01$
Affective Non-Conflict	96.67 (3.65)	89.05 (10.68)	3.09	$p < 0.01$

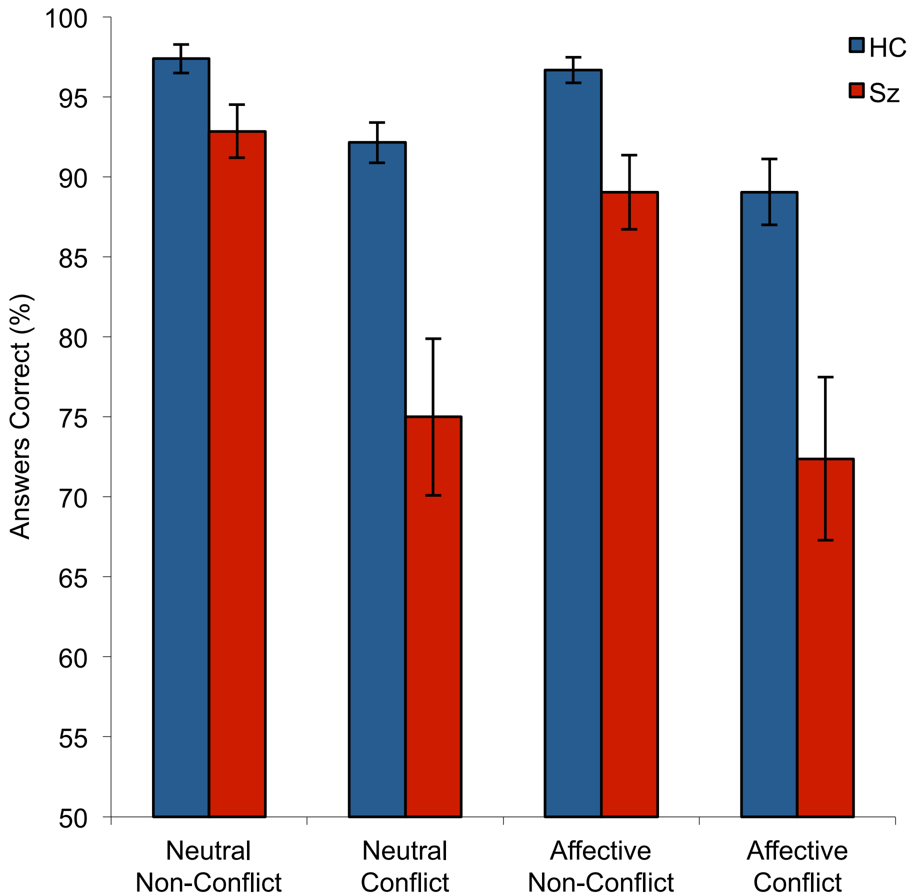

Figure 6.2 The mean percentage of correct responses by group (HC: healthy control; Sz: schizophrenia), conflict status (conflict and non-conflict), and salience (affective and neutral). Error bars show standard error of the mean (SEM). All between-group comparisons were statistically significant.

6.3.2.3 Within group t-tests

Mean values for all conditions are presented in Table 6.2. Both groups were less accurate in responding to Conflict than Non-Conflict conditionals (Controls: t[20] = -4.41, $p < 0.001$; Sz: t[20] = -4.18, $p < 0.001$), Affective-Conflict than Affective-Non-Conflict (Controls: t[20] = 3.47, $p <$; Sz: t[20] = 3.93, $p < 0.001$), Neutral-Conflict than Neutral-Non-Conflict (Controls: t[20] = 3.63, $p < 0.01$; Sz: t[20] = 4.10, $p < 0.001$), and Affective compared to Neutral conditionals (Controls: t[20] = -2.13, $p < 0.05$; Sz: t[20] = -2.33, $p < 0.05$). Healthy controls showed a trend towards poorer performance for Affective-Conflict compared to Neutral-Conflict (t[20] = 1.65, $p = 0.057$).

6.3.3 Functional imaging results

Performance of the conditional sentence task significantly activated a network of 3664 voxels, which included the subclusters described in Table 6.3, and illustrated in Figure 6.3.

The 2x2x2 (group by salience by conflict status) ANOVA of mean beta estimates (time bins four through six) showed a significant main effect of group, with greater activity for the healthy control group than schizophrenia group (Healthy Controls = 0.045 (SD = 0.015), Schizophrenia = 0.038 (SD = 0.015); ($F_{1,160}$) = 10.24, $p < 0.01$), and a main effect of salience, with greater activity for affective compared to neutral stimuli (Neutral =0.039 (SD = 0.015) , Affective = 0.044 (SD = 0.016); ($F_{1,160}$) = 4.93, $p < 0.05$). There was a trend towards significance for conflict status, with greater activity for conflict stimuli than non-conflict (Conflict = 0.043 (SD = 0.016), Non-Conflict = 0.039 (SD = 0.015); ($F_{1,160}$) = 3.37, p =0.068), and a trend for the interaction between conflict status and salience (($F_{1,160}$) = 3.66, p =0.057).

Table 6.3 Localisation of activations for task related activation clusters (voxels showing significant activity (t = 7.94, *p* = 0.00001, family wise error (FWE) correction for multiple comparisons), irrespective of group, and across both conditions).

Cluster Name	Peak MNI Coordinates (x, y, z)	Voxels	t =	*p* =
Occipital Cortex/Parietal Lobules	24, -100, -4	2160	20.99	0.000
Dorsal Anterior Cingulate Cortex	0, 16, 48	290	16.54	0.000
Prefrontal Cortex/Striatum	-20, 8, -4	803	14.26	0.000
Insula/Striatum	32, 24, -4	292	12.76	0.000
Prefrontal Cortex	56, 28, 24	76	12.16	0.000
Precentral Cortex	32, 0, 52	31	10.4	0.000
Hippocampus	24, -28, -4	9	9.47	0.000
Inferior Frontal Operculum	60, 16, 4	1	8.45	0.000
Hippocampus	-24, -32, -4	1	8.26	0.000
Fusiform Gyrus	44, -28, -16	1	8.12	0.000

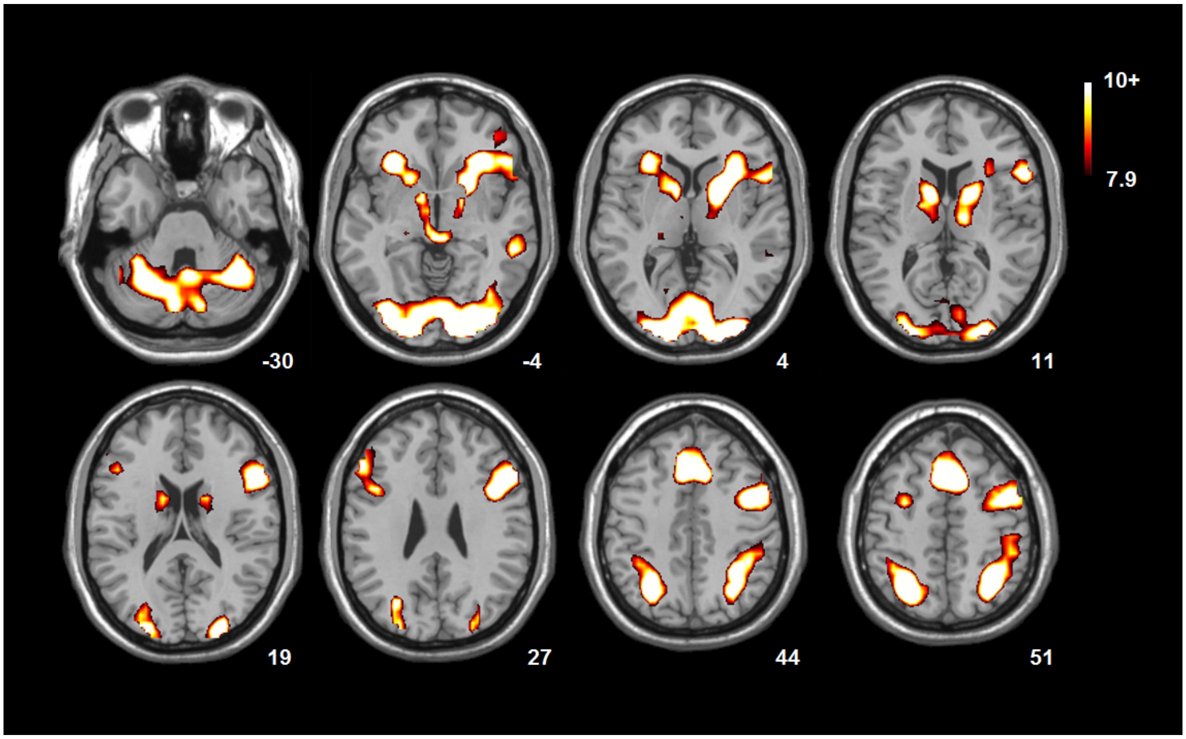

Figure 6.3 Mask of task related activation (corrected t = 7.94, p = 0.00001). This indicates significant voxels for time bins four through six from the FIR basis set, across all conditions, and irrespective of group membership.

Within-group t-tests indicated significantly greater activity for conflict stimuli compared to non-conflict for the healthy control group (Non-Conflict = 0.042 (SD = 0.013), Conflict = 0.048 (SD = 0.014); t(21) = 4.48, $p < 0.001$) and a trend for the schizophrenia group (Non-Conflict = 0.037 (SD = 0.013), Conflict = 0.039 (SD = 0.016); t(21) = 1.69, $p = 0.053$). Both healthy controls (Neutral = 0.042 (SD = 0.013), Affective = 0.048 (SD = 0.014); t(21) = 5.34, $p < 0.001$) and the schizophrenia group (Neutral = 0.036 (SD = 0.014), Affective = 0.039 (SD = 0.015); t(21) = 2.83, $p < 0.05$) showed greater activity for affective compared to neutral stimuli. In summary, both groups showed an increase in activity for conflict compared to non-conflict stimuli, and an increase in activity for affective compared to neutral stimuli.

Between-group t-tests showed that the healthy control group had greater activity than the schizophrenia group for conflict stimuli (t(40) = 2.03, $p < 0.05$), but not non-conflict stimuli (t(40) = 1.27, $p = 0.106$). This difference reflects the significantly greater increase in activity for conflict stimuli compared to non-conflict stimuli (Conflict minus Non-Conflict) for the healthy control group compared to the schizophrenia group (t(40) = 2.33, $p < 0.05$). Healthy controls also showed greater activity than the schizophrenia group for affective stimuli (t(40) = 1.97, $p < 0.05$), but not neutral stimuli (t(40) = 1.36, $p = 0.091$). This reflects the greater increase in activity for affective compared to neutral stimuli (Affective minus Neutral) for the healthy control group compared to the schizophrenia group (t(40) = 1.9, $p < 0.05$).

The schizophrenia group showed significant correlations between performance on the conflict condition and BOLD activity associated with the conflict condition for the entire network (r[21] = 0.422; $p < 0.05$; Figure 6.4). There was no significant correlation for the healthy control group (r[21] = -0.04; $p = 0.432$).

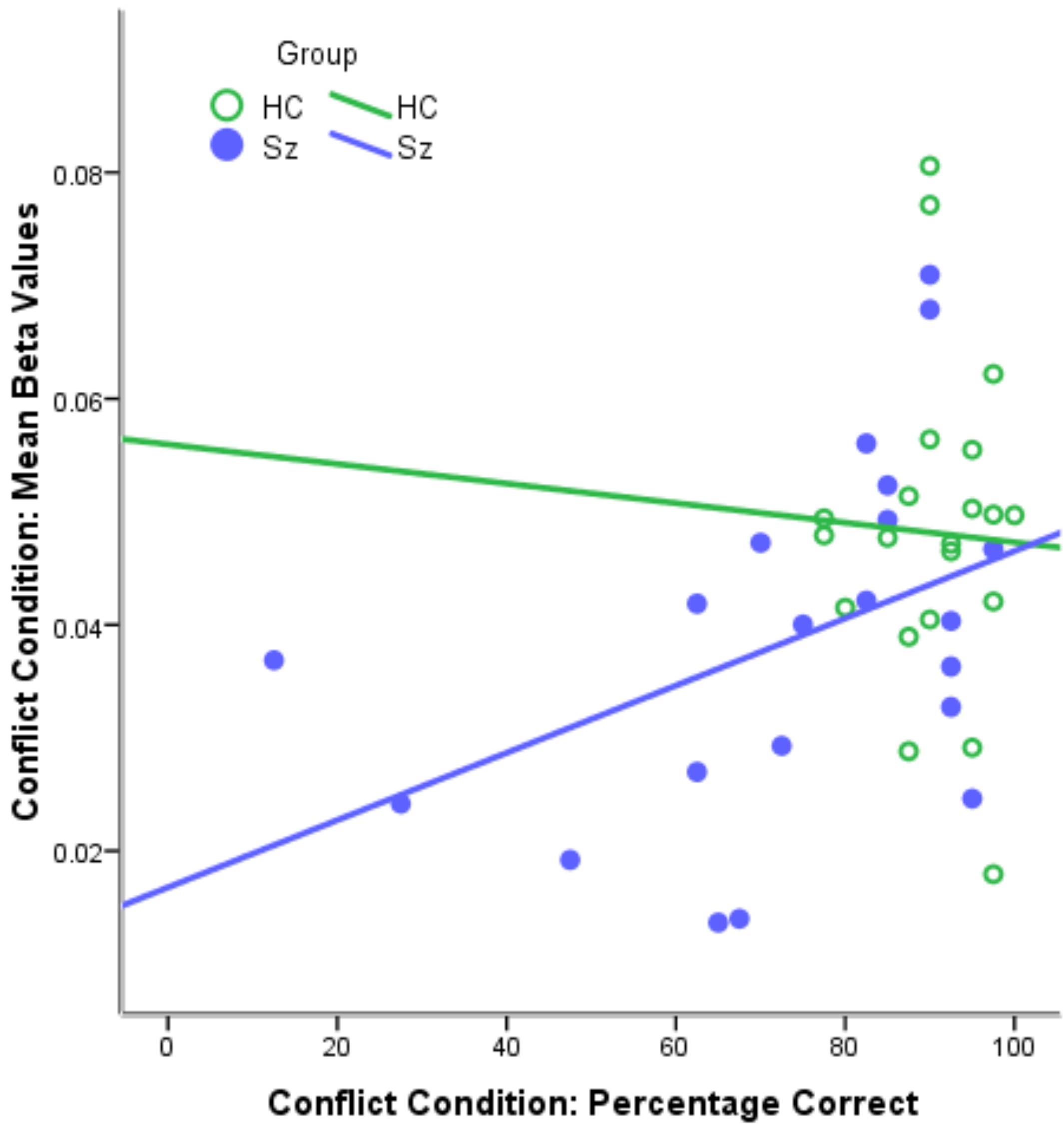

Figure 6.4 Correlations between performance on the conflict condition and the mean beta values for the conflict condition for the whole mask. This schizophrenia group showed a significant correlation (r[21] = 0.422; $p < 0.05$); the healthy control group did not (r[21] = -0.04; $p = 0.432$).

6.4 Discussion

The Dual-Stream Modulation Failure (DSMF) model of delusions suggests two processing aberrations that may contribute to delusion formation and maintenance in schizophrenia: a failure of cognitive conflict to adequately increase deliberative, Stream 2 processing (CMF) and an accentuated emotional modulation (AEM) away from Stream 2 and towards non-deliberative, Stream 1 processing. These modulation deficits may occur in tandem or separately, leading to an under-recruitment of Stream 2 processing and/or an increase in (or relative failure to suppress) Stream 1 processing. This creates a cognitive environment were erroneous, intuitive beliefs are more likely to be endorsed, and then endure, despite minimal evidential support.

The data presented replicate and extend previous findings in support of the conflict arm of the DSMF model. The interference of believability with assessments of logical validity is a well-documented phenomenon in healthy controls (Goel & Dolan, 2003a; Evans, Barston & Pollard, 1983; Evans, 1989; Morley, Evans & Handley, 2004; De Neys, 2006). CMF suggests that this effect will be exaggerated in people diagnosed with schizophrenia (Speechley & Ngan, 2008; Speechley et al., 2010). As in Chapter Five, the schizophrenia group exhibited a significantly greater decrease in performance than healthy controls for the conflict condition compared to the non-conflict. This study extends previous findings by providing neurophysiological data consistent with the processing differences predicted by CMF. As expected for a cognitively demanding task, participants demonstrated a central executive network (CEN) (Cabeza & Nyberg, 2000a; Cabeza & Nyberg, 2000b)/task-positive functional network (Fox, et al., 2005)/multiple demands network (Duncan & Owen, 2000) pattern of activation, consistent with other studies utilising deductive reasoning paradigms (e.g., Goel, Gold, Kapur & Houle, 1997; Goel, Gold, Kapur & Houle, 1998; Osherson et al., 1998), and including nodes associated with both conflict processing (dACC) and deliberative reasoning (L/DLPFC). Consistent with conflict modulation, namely, an increase in deliberative processing when presented with a conflict stimulus (Botvinick, Braver, Barch, Carter & Cohen, 2001; Botvinick, Cohen & Carter, 2004; Luks, Simpson, Feiwell & Miller, 2002; Gehring & Taylor, 2004; Hayden & Platt, 2006; Behrens, Woolrich, Walton & Rushworth, 2007; Woodward, Metzak, Meier & Holroyd, 2008), the healthy control group showed a significant increase in activity in this network for the conflict condition compared to the non-conflict. A significantly smaller increase was observed in the schizophrenia group, consistent with research demonstrating attenuated dACC activity for schizophrenia patients in response to conflict stimuli in the Stroop task (Carter, Mintun, Nichols & Cohen, 1997) and for error commission in the Go/No-Go task (Laurens, Ngan, Bates, Kiehl & Liddle, 2003). Within the conflict arm of the model, the increase in activity for the conflict condition may represent enhanced engagement of Stream 2 processes when faced with cognitive conflict. The failure of the schizophrenia group to enhance activity in this network to the same degree as healthy controls may be the physiological basis for the greater decrease in performance for the conflict condition displayed by the schizophrenia group. The interpretation that an increase in CEN activity when confronted with cognitive conflict corresponds to an increase in Stream 2 processing that reduces the likelihood of believability lead errors is further supported by the positive correlation between the magnitude of activity in this network and task performance for the conflict condition in the schizophrenia group. The lack of a correlation for the healthy control group may reflect the lack of variance in the data for this group (nearly all controls showed both high levels of performance and high conflict condition activity).

This is the first study investigating the emotional modulation arm of the DSMF model. Emotional modulation suggests that the belief-bias effect should be greater for affective stimuli than more neutral stimuli owing to a greater bias away from deliberative Stream 2 and towards automatic Stream1 processing. AEM suggests that this effect will be greater for people diagnosed with schizophrenia than for healthy controls. However, while there was a significant main effect of conflict status, there was no significant main effect of salience or interaction of salience with conflict status. Exploratory t-tests suggested that both groups experienced marginal decreases in performance for affective compared to neutral stimuli, with only the healthy control group showing an additive effect of conflict and affect on conditional reasoning performance, suggestive of the predicted emotional modulation effect, i.e., a greater drop in performance for conflict stimuli that were affective compared to neutral.

We predicted that emotional salience would decrease activity in putative Stream 2 processing areas (e.g., dACC and frontal cortex). However, both groups showed the reverse pattern of results, with greater CEN activity for emotionally salient stimuli than for neutral. This was somewhat unexpected and is difficult to interpret given Goel and Dolan's (2003b) comparison of neutral syllogisms with emotionally salient syllogisms where L/DLPFC activation was attenuated for emotionally salient stimuli compared to neutral.

There is ample evidence of emotionally salient content or emotional states interfering with deductive reasoning (Blanchette, 2006; Blanchette & Campbell, 2005; Blanchette & Leese, 2011; Blanchette & Richards, 2004; Channon & Baker, 1994; Kemp, Chua, McKenna & David, 1997; Oaksford, Morris, Grainger & Williams, 1996). Therefore, the behavioural and fMRI results of the current study require a consideration of whether the designed salience difference between stimuli conditions was successfully achieved. An examination the fMRI data, which indicated greater rostral ACC activity for affective compared to neutral conflict, suggests that it was (see Appendix V). However, a recent study by Blanchette and Leese (2011) found that physiological arousal (as measured by skin conductance responses) was more robustly associated with the impact of emotion on deductive reasoning than participants' subjective affective ratings of stimuli. Given that the affective stimuli set in our study was selected in piloting via subjective ratings of arousal and salience, it is possible that the emotionally salient stimuli in our study were not sufficiently personally salient or arousing enough to induce the anticipated effect. A sufficient threshold of intensity may need to be exceeded before the effect will be seen, particularly as increased cognitive demands are associated with decreases in activity in regions of the brain associated with processing affect (e.g., Simpson et al., 2001a; Simpson et al., 2001b). Further, while the fMRI data suggests that we achieved an affect difference between conditions, we may also have underestimated the strength of the belief-bias effect achieved by the less emotive, but potentially equally salient real world content of the "neutral" condition. For example, while arousal may potentially be higher when required to endorse a stimulus ending with, "no rapists are criminals", it is difficult to say that it would be any easier to overcome the belief-bias induced by a more neutral statement like, "no fish can swim", for which endorsement requires violation long held basic knowledge concerning the rules of the natural world.

Some recent research has begun to question the status quo regarding how emotional salience may interact with the ability to reason logically. For example Goel and Vartanian (2011) present data suggesting that negative emotions induced by inflammatory or politically incorrect content (as utilised in the present study) may attenuate the belief-bias effect in syllogistic reasoning. Goel references the Affect Infusion Model (AIM; Forgas,

1995) in accounting for this effect. The AIM model suggests that negative affective responses may, under some conditions, increase vigilance and subsequently, facilitate formal reasoning. It is possible that the increased activity in putative Stream 2 areas for affective content compared to neutral in the current study reflects such an effect, despite there being little difference between conditions behaviourally.

In addition to the potential limitations of our design in probing the AEM arm of the DSMF model, it should be noted that the schizophrenia group had 1.5 fewer years of education than the control group, with 13.8 (SD = 2.2) years of education to the 15.2 (SD = 2.6) of the controls. This represents a smaller difference between groups than in the study described in the previous chapter where the schizophrenia group had 12.7 (SD = 2.3) years of education and the control group 16.2 (SD = 3.1). Further, unlike the previous study, there were no differences in either QUICK (a proxy measure of current IQ) or NART (a proxy measure of premorbid IQ) scores, and neither group displayed a correlation between years of education and performance. Thus, this study recruited a more educated patient group and less educated control group than the previous study, with correlations between years of education and performance disappearing while the greater drop in performance for the schizophrenia group for conflict compared to non-conflict stimuli remained. While the difference in years of education between groups may have contributed to a general group difference in performance, it is difficult to credit a 1.5 year difference in general education with conferring a specific ability to inhibit beliefs in decision-making when healthy controls are confronted with belief-logic conflicts.

6.5 Exploratory analysis

When identifying a network of significant activations for assessing our hypotheses, there were also regions with significant negative beta values that merit consideration as potential targets for future studies (see Appendix VI). The largest region of “deactivation” was in the VMPFC, with smaller clusters in the precuneus, fusiform gyrus, DLPFC, and ventral posterior cingulate cortex, in a pattern suggestive of the default mode network (DMN; Gunsard & Raichle, 2001; Raichle et al., 2001).

DMN research consistently identifies three core regions: VMPFC, posterior cingulate cortex (PCC) and inferior parietal lobule (IPL) (Buckner, Andrews-Hanna & Schacter, 2008). Less robust findings include the hippocampal formation and a lateral temporal cortex region extending into the temporal pole. When engaged in cognitively demanding tasks the DMN deactivates, while the CEN increases in activity (Greicius, Krasnow, Reiss & Menon, 2003; Fransson, 2005; Fox et al., 2005). One theory of DMN function, with emphasis on the VMPFC node, is that it may be involved in self-reflective thought of a social and emotionally salient nature (Gusnard, Akbudak, Shulman & Raichle, 2001; Gusnard & Raichle, 2001; Mitchell, Macrae & Banaji, 2006) or undirected, spontaneous thought (Shulman et al., 1997; Mazoyer et al., 2001; Raichle et al., 2001), such as “mind-wandering” (Mason et al., 2007; Christoff, Gordon, Smallwood, Smith & Schooler, 2009). The potential role of the medial temporal lobe in the DMN in this context may be to retrieve memories and associations based on personal past experiences (Henson, Rugg, Shallice, Josephs & Dolan, 1999; Eldridge, Knowlton, Furmanski, Bookheimer & Engel, 2000; Wheeler & Buckner, 2004; Yonelinas, Otten, Shaw & Rugg, 2005; Wagner, Shannon, Kahn & Buckner, 2005). VMPFC activity decreases when a participant is engaged in cognitively demanding activities (Shulman et al., 1997), and increases when an emotional response is elicited (Pardo, Pardo & Raichle, 1993; George et al., 1995; Lane, Reiman, Ahern, Schwartz & Davidson, 1997; Lane et al., 1997; Whalen et al., 1998; Ploghaus et al., 1999). Further, emotional experience appears to decrease task-related deactivation of DMN (Gusnard, Akbudak, Shulman & Raichle, 2001; Simpson, Snyder, Gusnard & Raichle, 2001; Simpson, Drevets, Snyder, Gusnard & Raichle, 2001), and inadequate DMN suppression has been associated with poorer cognitive performance in healthy controls (Daselaar, Prince & Cabeza, 2004; Weissman, Roberts, Visscher & Woldorff, 2006; Mason et al., 2007; Sonuga-Barke & Castellanos, 2007), potentially indicating the interference of spontaneous, self-referential thought.

There is mounting evidence of dysfunctional DMN activity in schizophrenia, with accounts either indicating overactivity or a relative failure to deactivate the DMN (Pomarol-Clotet et al., 2008; Whitfield-Gabrieli et al., 2009; Park et al., 2009; Salgado-Pineda et al., 2011). This phenomenon has been associated with poorer task performance in patients with schizophrenia (Harrison, Yucel, Pujol & Pantelis, 2007) and may be correlated with positive symptoms (Garrity et al., 2007). One study identified the VMPFC in particular as showing reduced suppression in patients and their relatives while performing a working memory task (Whitfield-Gabrieli et al., 2009), with better task performance being correlated with greater VMPFC suppression. This data has been used to support the suggestion that inadequate DMN suppression may indicate impairment in the interaction between personal thoughts/feelings and the external world, disrupting cognitive task performance and potentially contributing to the disturbances of thought characteristic of schizophrenia (Buckner, Andrews-Hanna & Schacter, 2008; Whitfield-Gabrieli et al., 2009).

Given the role of the VMPFC in processing emotionally salient stimuli, its association with belief-biased, Stream 1 responses, and its anti-correlation with CEN activity during cognitive tasks, the DMN may be an appropriate target network for future studies assessing emotional modulation towards Stream 1 in the context of the DSMF model. For example, the DMN literature points to the role of the hippocampus in retrieving memories and associations based on personal past experiences (Henson, Rugg, Shallice, Josephs & Dolan, 1999; Eldridge, Knowlton, Furmanski, Bookheimer & Engel, 2000; Wheeler & Buckner, 2004; Yonelinas, Otten, Shaw & Rugg, 2005; Wagner, Shannon, Kahn & Buckner, 2005), and the VMPFC in mediating judgments made on stimuli with social or emotional content (Gusnard, Akbudak, Shulman & Raichle, 2001; Mitchell, Macrae & Banaji, 2006). Constructing a DSMF hypothesis with the DMN as a target network for examining the influence of emotional salience on biasing processing away from Stream 2 and/or towards Stream 1 one may suggest that inadequate DMN suppression may indicate associative, experiential Stream 1 interference with deliberative Stream 2 processes, which may be even more likely when considering emotionally salient stimuli. In sum, the DMN literature suggests that emotional modulation and impaired Stream 1 inhibition may be evidenced by reduced DMN deactivation for emotionally salient stimuli compared to neutral. AEM suggests that this difference would be greater for the schizophrenia group.

Consistent with emotional modulation, namely an increase in associative, Stream 1 processing when considering emotionally salient stimuli, both groups suppressed DMN activity less for emotionally salient stimuli than for neutral (see Appendix VI). However, there was no evidence of AEM in the schizophrenia group as there was no difference in deactivation between groups for emotionally salient stimuli. However, there was a main effect of group, with the schizophrenia group deactivating the DMN less than healthy controls. This is consistent with previous evidence of inadequate DMN suppression in schizophrenia (Buckner, Andrews-Hanna & Schacter, 2008; Pomarol-Clotet et al., 2008; Whitfield-Gabrieli et al., 2009; Park et al., 2009; Salgado-Pineda et al., 2011), which may correspond to difficulty in shifting cognitive resources from internal thoughts and feelings towards external task demands, potentially heightening feelings of self-relevance in people with delusions (Whitfield-Gabrieli et al., 2009).

6.6 Conclusion

The current results provide further behavioural support for both conflict modulation in healthy controls and CMF in schizophrenia. Additionally, this study indicates that conflict modulation towards Stream 2 processing may be associated with an increase in CEN activity, which includes regions previously identified as involved in conflict detection and deliberative processing (i.e., dorsal anterior cingulate cortex and frontal cortex). CMF in schizophrenia may be the result of a failure to adequately engage this network, increasing the likelihood of erroneous judgments when faced with belief-logic conflicts. There was little evidence for emotional modulation in healthy controls, and no evidence for AEM in the schizophrenia group, either behaviourally or in the fMRI data. One possibility is that the emotionally salient stimuli were not personally salient or arousing enough to sufficiently induce the anticipated effect. Future studies could address this issue by including stimuli that relate thematically to the specific delusional beliefs of each schizophrenia group participant, and personally tailoring the emotionally salient stimuli set to each healthy control participant by using a questionnaire method to individualise the stimuli. An exploratory analysis of the significant negative beta estimates indicated a DMN pattern of activity that may be a fruitful target for future research on the emotional arm of the DSMF model. This data provided some preliminary support for the notion of emotional modulation in both groups, as suggest by decreased DMN deactivation for affective compared to neutral stimuli.

Chapter Seven: General discussion

7.1 Introduction

This thesis presents studies adding to our understanding of previously identified cognitive biases in schizophrenia. It also outlines the development of a novel model of delusions in schizophrenia and the first data papers exploring this new model. Unlike many well-supported cognitive theories detailing reasoning biases that may contribute to or characterise delusions, the dual-stream modulation failure (DSMF) model indicates decision-making mechanisms that may underlie delusion formation and maintenance, and that may be mapped to regions of the brain.

In addition to a brief summary of the preceding data, this discussion will return to the review of the cognitive literature on delusions presented in the introduction (Chapter One) for reconsideration within the context of the DSMF model. However, it should be emphasized that DSMF was developed to account for delusions, and not to account for the various cognitive biases suggested by the existing delusions literature. To the extent that all are attempts to identify reasoning aberrations that may contribute to delusions there should be some concordance or overlap between other cognitive approaches and components of the DSMF model.

7.2 Thesis research summary

7.2.1 Cognitive biases data summary

Two particularly well-studied and well-supported cognitive biases in schizophrenia are the jumping-to-conclusions bias (JTC) and the bias against disconfirmatory evidence

(BADE). While much has been said previously about these biases, the research presented in chapters two and three offers new ways of viewing this literature.

The JTC research presented in Chapter Two aimed to return to Huq et al.'s (1988) original approach of considering the study design and results from a Bayesian perspective, though made some key modifications to the task: replacing beads and jars for potentially less abstract stimuli (fish and lakes), and utilising a separate rating scale for each of the two response options, rather than the single, bipolar scale typically employed. Consistent with previous research, we showed that, from a Bayesian perspective, healthy controls may be more conservative reasoners than people diagnosed with schizophrenia, though it is possible that this is a more ecologically valid approach to everyday reasoning that may be protective against delusion formation. Unlike previous research, our results did not allow us to endorse the suggestion that delusional participants were "more Bayesian" (and by implication, more rational) in their reasoning than controls. Later in a series of same colour fish catches, people with delusions did show a maximal level of confidence that was closer to that predicted by the Bayesian formula, though after a single catch (i.e., at the beginning of the series) the delusions group was the least Bayesian of the groups, showing far greater confidence in their decisions than the other groups and than would be predicted by the Bayesian formula.

The most significant observation of our JTC research was provided through the utilisation of separate rating scales for each lake. This allowed us to propose a modification to the typical JTC interpretation, which we termed the "hypersalience of evidence-hypothesis matches" (Speechley, Whitman & Woodward, 2010). This describes our observation that the severely delusional schizophrenia group showed a tendency to overrate any option supported by the current evidence, while showing comparable responses to controls for options not supported by the current evidence. Previous research utilising an integrated A–B continuous scale appears to have misinterpreted this response tendency as a "bias towards disconfirmatory evidence" (Garety, Hemsley & Wessely, 1991), given what appeared to be greater downward over-adjustments in probability estimates for schizophrenia patients compared to healthy controls following a single instance of disconfirmatory evidence during the beads task. Our two-scale variant beads task suggests that it may be less a case of enhanced down-rating of a previously supported option, and more a case of too readily endorsing whatever response option is best supported by the current stimulus in beads-type tasks. Further, this study suggested that the beads literature need not invoke the presence of two different biases evident at different points in a series of bead draws, i.e., JTC when overconfident responses are made at the beginning of a series, and a bias towards disconfirmatory evidence when overadjustments are made later in a series. The hypersalience of evidence-hypothesis matches suggests that there is only one bias evident in this paradigm: the tendency of people with delusions to show a greater preference for whichever option is supported by the current incoming data, while simultaneously showing normal ratings for the less supported option.

The BADE research presented in Chapter Three represented the first study to utilise a multivariate analysis of the BADE data using all available information from the task (i.e., lures, true interpretations, and absurd interpretations). This allowed all ratings to contribute to interpretation of the cognitive underpinnings of the evidence integration necessary in the BADE task. The results replicated previous support for BADE in delusions for the lure items (i.e., an inadequate downward adjustment of plausibility ratings when necessitated by incoming disambiguating evidence), but suggested that BADE is caused by a more general effect that also affects ratings of the absurd items, and reciprocally, the true items.

Specifically, the principal component analysis carried out on all measures determined that two independent cognitive processes appear to combine to determine all responses on the BADE task: Evidence Integration and Believability, with only the former discriminating between the severely delusional schizophrenia group and all other groups. Thus, Evidence Integration appears to be functioning sub-optimally in severely delusional schizophrenia patients, resulting in the BADE effect.

A limitation of these two studies was the small sample size for the severely delusional schizophrenia group. However, the effects reported were only detectable in the most severely delusional people, and it is possible that inconsistency in previous research on these biases was due to the use of lower cut-offs for inclusion in the delusion group, resulting in the averaging together of patients experiencing milder levels of delusions with those experiencing severe delusions. Our results suggest that future studies should aim to recruit sufficiently large samples of severely delusional participants to avoid this practice.

7.2.2 DSMF theory and data summary

One of the primary motivations for this thesis was to develop the DSMF model of delusions (Chapter Four), design experiments to determine whether the two proposed modulator deficits (conflict modulation failure (CMF) and accentuated emotional modulation (AEM)) were evident in schizophrenia, and identify regions of the brain that may underlie these decision-making deficits (Chapter Five and Chapter Six).

The DSMF model is comprised of two decision-making processes (Stream 1 and Stream 2) and two modulators (conflict and emotion/salience) that influence the balance between these two modes of processing in a given situation. The studies described in the previous two chapters attempted to engage each of the modulators to manipulate the balance between Stream 1 and Stream 2 reasoning. CMF and AEM were proposed as potential modulator dysfunctions that, together or individually, may aberrantly tip the balance of reasoning towards Stream 1 and away from Stream 2 in schizophrenia, increasing the likelihood of delusional ideation.

The conflict arm of the DSMF model suggests that when there is a cognitive conflict, reasoning should be modulated towards Stream 2's more deliberative processes, increasing the likelihood of a judgment in keeping with the available evidence. A failure to detect conflict and/or to adequately tip the balance of reasoning towards Stream 2 (CMF) may enable erroneous beliefs to be accepted and maintained in schizophrenia despite the availability of convincing evidence to the contrary.

The CMF hypothesis was tested in both data papers, and received the strongest support of the two proposed modulator aberrations. Using a conditional reasoning paradigm that placed belief in conflict with logical validity, we found that people with schizophrenia showed a greater drop in performance than healthy controls when there was a cognitive conflict. Functional magnetic resonance imaging indicated that this was associated with a smaller increase in activity in a network (CEN) that included regions of the brain previously associated with conflict detection/modulation (dACC) and deliberative reasoning (frontal cortex). Further, the performance of the schizophrenia group for conflict stimuli was positively correlated with activity in this network, such that less activity in the predicted regions was associated with a greater likelihood to make erroneous, belief-biased decisions when faced with a belief-logic conflict.

The emotional salience arm of the DSMF model suggests that salience, particularly emotional salience, may modulate reasoning away from Stream 2 and towards the more automatic, associative processes of Stream 1. This stream may generate feelings of "felt rightness" (Moscovitch & Winocur, 2002), rather than suggesting interpretations based on deliberative assessments. Stream 1 may actually be the more effective mode of processing in some situations, as the more precise, deliberative processes of Stream 2 may have a smaller capacity than Stream 1, which can rapidly generate impressions on larger amounts of information (Dijksterhuis, 2004; Dijksterhuis & van Olden, 2006). Dijksterhuis' "shopping studies" demonstrated how these faster, more automatic forms of decision-making can be more accurate than deliberation when making decisions regarding consumer choices of high complexity, and often result in higher levels of satisfaction in the chosen purchases. However, Stream 1 may not be as adaptive in situations where evidence evaluation is necessary. In such instances "impressions" may not provide a sufficient consideration of the available evidence, and may increase the likelihood of erroneous assessments. Further, emotional salience may engender a stronger bias towards a particular interpretation, irrespective of the available evidence, which will be less likely to be attended to adequately when Stream 1 processing is enhanced.

Psychosis has been associated with accentuated emotional experience (Nayani & David, 1996; Freeman, Garety & Kuipers, 2001), particularly with regards to themes congruent with an individual's delusional beliefs (Rossell, Shapleske & David, 1998). As Kraeplin (1921) suggested, delusions appear "as the morbidly transformed expression of the natural emotions of the human heart", with the content of delusional beliefs reflecting the salient themes of healthy mental life. A delusion may start as a personally meaningful, salient belief that becomes imbued with aberrant salience during delusion formation. Once an overvalued idea becomes hypersalient, aberrantly accentuated emotional modulation (AEM) may serve to further increase the likelihood that Stream 1 is favoured over Stream 2, regardless of the specific processing needs of a given situation. Thus, erroneous, but belief-consistent interpretations may be accepted more readily, and persist more tenaciously, despite poor concordance with the available evidence.

The AEM hypothesis was only tested in Chapter Six, where both emotionally salient and neutral content was included in our conditional reasoning paradigm. The expectation was that people with schizophrenia would show a greater response to the emotionally salient stimuli than healthy controls. Behaviourally, this was anticipated to be expressed as an even greater number of errors for emotionally salient conflict stimuli than neutral conflict stimuli for the schizophrenia group compared to the healthy control group. Given our study design we restricted our *a priori* fMRI hypotheses to the deliberative Stream 2 side of the DSMF model, i.e., the expectation that emotional salience would bias processing away from putative Stream 2 regions. AEM was not supported by either the behavioural or fMRI data, with the results only providing support for a CMF effect, regardless of content type.

An exploratory analysis of significant negative beta values suggested the default mode network (DMN) as a potential future target for both emotional modulation and Stream 1 processing. This notion is supported by previous research implicating the ventromedial prefrontal cortex (VMPFC) in both belief-biased responding (Goel & Dolan, 2003a) and the processing of emotionally salient stimuli (Goel & Dolan, 2003b). Examination of this network provided some preliminary support for emotional modulation in both groups, with the fMRI data showing less DMN deactivation for emotionally salient stimuli compared to neutral. Further, the behavioural data gave some indication of poorer performance for emotionally salient stimuli compared to neutral for both groups, with the healthy control group also showing marginally poorer performance for emotionally salient conflict stimuli compared to neutral conflict stimuli.

In summary, using the current conditional reasoning paradigm we found evidence for conflict modulation, but only weak evidence for emotional modulation of dual-stream processing in healthy controls. DSMF suggests that delusions may be the result of a shift in the balance between Stream 1 and Stream 2 processes, such that Stream 1 endorsed interpretations are insufficiently moderated by Stream 2 reasoning. The proposed source of this dual-stream imbalance in schizophrenia is CMF and/or AEM. The studies presented in chapters five and six provided support for CMF in schizophrenia, but there was no evidence for AEM. However, there was some preliminary support for emotional modulation in the healthy control and schizophrenia groups, with emotionally salient stimuli reducing the degree of DMN deactivation compared to neutral stimuli.

7.3 Dual-stream modulation failure and cognitive biases in schizophrenia

7.3.1 The bias against disconfirmatory evidence

BADE research (e.g., Chapter Three) represents an experimental demonstration of the failure to adjust beliefs “despite what constitutes incontrovertible and obvious proof or evidence to the contrary” (American Psychiatric Association, 2000), and indicates that this bias extends beyond the content and context of the delusional belief to delusion neutral material. BADE appears to be a specific reasoning characteristic that may be associated with delusion maintenance, but does not offer an underlying mechanism that can account for the expression of the cognitive bias itself. A relative insensitivity to belief inconsistent information or deficit in evidence integration, as demonstrated by BADE research, can be accounted for by the conflict arm of the DSMF model of delusions. CMF indicates that a conflict between a belief and disconfirmatory evidence fails to adequately modulate reasoning towards deliberative Stream 2 processes, decreasing the influence of disconfirmatory evidence on decision-making and increasing the likelihood that an erroneous belief will endure, uncorrected.

7.3.2 Probabilistic reasoning and the beads task

The literature on JTC (including the "hypersalience of evidence–hypothesis matches" study presented in Chapter Two) paints a consistent picture; people with delusions require less evidence before making a decision and, on a trial-by-trial basis, show increased confidence in response options than non-delusional patients and healthy controls. The liberal acceptance (LA) hypothesis suggests that this may be due to a lowered threshold for hypothesis acceptance in schizophrenia, while the hypersalience theory suggests that aberrant salience may increase the degree to which even a poorly supported option is favoured. All have been used to demonstrate that weakly supported or erroneous interpretations are considered more favourably in schizophrenia, and so may be a contributing factor in delusion formation.

Reasoning biases identified through use of the beads task have tended to provide accounts of delusion formation alone, while DSMF provides a mechanism for both delusion formation and maintenance. CMF provides a better account for BADE than JTC type biases, though CMF could contribute to prematurely early decisions or an increased level of confidence in poorly supported response options in some circumstances. For example, early decisions where evidence is mixed (e.g., bead draws of pink, green, pink or green, pink, pink) may indicate a relative insensitivity to conflicting information, given the expectation that many individuals would request more evidence before making a decision in such scenarios. The paradigmatic JTC response of making a decision following a single bead is discussed in Chapter Two, and described as indicating a hypersalience of evidence-hypothesis matches effect in schizophrenia. In the context of AEM, salience is described as being accentuated, biasing processing towards more reactive, non-deliberative Stream 1 processes. This may allow even limited evidence to be experienced as salient enough to elicit an unusually early or overconfident response.

Given that incorrigibility may be considered the defining feature of delusions, the beads literature is only partially consistent with what is known about delusions; the early acceptance of hypotheses seems to offer a means by which to understand how an erroneous idea may be more likely to be accepted, but a greater tendency to switch positions, as suggested by the "disconfirmatory bias" or trial-by-trial "hypersalience of evidence–hypothesis matches" effect, appears difficult to reconcile with the apparent tenacity of delusions. The readiness with which options are accepted and rejected in these probabilistic tasks seems to suggest either ambivalence, consistent with Bleuler's (1911) four A's of schizophrenia (association, affect, ambivalence, and autism), or an inadequate weighting of previously received evidence when considering new information. Further work may be required to fully investigate this little discussed aspect of the beads literature with regards to what it can tell us about delusions. Perhaps the best account for this discrepancy is provided by Garety and Freeman (1999), who suggest that making, abandoning, and making a new hypothesis on the basis of minimal evidence may only apply to neutral content, as in the abstract situation provided by the binary choice beads task, where the stimuli hold no personal relevance to the participants.

7.3.3 Perceptual disorder and the two-deficit model

In the perceptual disorder account, Maher (1974) proposed that delusions were the result of a normally functioning reasoning system attempting to explain anomalous perceptual experiences. This theory may explain why certain explanations are favoured for some delusions, but does not account for why more plausible alternative explanations are not ultimately chosen, and why delusional beliefs are so resistant to contradictory evidence. The DSMF model does not require the presence of perceptual anomalies in delusion formation, but it also does not preclude the possibility that perceptual disturbances may contribute to delusional ideation, in some cases. It diverges most significantly from Maher's account in its emphasis on an ongoing aberration in decision-making, providing mechanisms (dual-stream modulator dysfunctions) to account for why an erroneous belief is adopted over other more parsimonious explanations, and why such a belief is so tenaciously held onto.

While perceptual disorder account may, in some cases, provide a viable explanation for the formation of a delusional belief, robust evidence of reasoning biases in people with delusions (e.g, JTC and BADE) suggests that Langdon and Coltheart's (2000) "two-deficit" model may have more explanatory power. In addition to a perceptual deficit, the two-deficit model indicates that there must also be a "failure of normal belief evaluation". Langdon and Coltheart suggest that this deficit may take the form of a failure to prevent automatic, belief-biased responses from interfering with a more critical consideration of the available evidence. DSMF offers a specific model of this second deficit. Consistent with Langdon and Coltheart's suggestion of automatic processes interfering with critical reasoning, DSMF suggests that delusions are the result of an imbalance between Stream 1 and Stream 2 decision-making processes. DSMF goes further though, suggesting that the aberrant interaction between these two processes may be due to the dual-stream modulator anomalies CMF and AEM.

7.3.4 Aberrant salience

The aberrant salience model connects the expression of delusions with biological function (specifically, a dopamine neurotransmitter aberration), while DSMF connects the expression of delusions with brain function, from a cognitive perspective. The difference in approaches may offer room for both to inform each other. However, there are some elements of each model that may not be reconcilable. Kapur suggests two stages in delusion formation: dysregulated dopamine transmission creating aberrant saliences where there should be none, and the individual imposing top-down cognitive explanations on these aberrant saliences, coloured by the themes that are already relevant to the individual. This treatment of salience in delusion formation differs from AEM in the DSMF model, which implies that what is already salient to an individual may become imbued with exaggerated salience in psychosis, perhaps due to dysregulated dopamine transmission. This aberrantly tips the balance of reasoning towards Stream 1, which may operate more on gut feelings of what "feels right" based on existing saliences, diminishing critical evidence evaluation from Stream 2 processes. Thus, the key difference between the two models is that instead of creating saliences, dysregulated dopamine transmission in DSMF may serve to heighten what is already salient, biasing processing towards Stream 1 and away from Stream 2.

With regards to why a certain belief is adopted and maintained, Kapur's model indicates that anxiety reduction/insight relief/psychotic insight is achieved by generating an explanation for the anomalous experiences created by dysregulated dopamine transmission. This is a similar explanation as offered by Maher's perceptual abnormality account of delusions; the reduction of anxiety provides reinforcement for the acceptance and maintenance of the delusional belief. However, this explanation does not account for why more plausible explanations are discarded or ignored, both initially, and continuously during delusion maintenance. The role of anxiety in delusions is treated quite differently within the DSMF framework. Here, anxiety may be an indicator of accentuated emotion, which exerts an aberrantly powerful bias towards Stream 1 and away from Stream 2 (AEM), increasing the likelihood that erroneous explanations will be accepted and maintained. This process may be exacerbated by the reduced influence of cognitive conflict on reasoning (CMF).

7.4 Future directions for DSMF

The research studies exploring DSMF in this thesis operated within the constraints of a single experimental paradigm, and found support for conflict modulation and CMF, with only preliminary evidence for emotional modulation. Future directions for testing the DSMF model must include further attempts to verify, refute or modify the AEM arm of the model. Two possibilities present themselves: (1) a redesign of the current conditional reasoning paradigm that attempts to utilize content that is more personally salient and arousing (for the schizophrenia group, this may mean the inclusion of content that taps into each individual's delusional belief system). (2) Searching for or generating a more appropriate paradigm to investigate AEM.

While the DSMF model is a general psychological model of reasoning that taps into cognitive operations shared between deductive and inductive reasoning, we believe that deductive reasoning paradigms offered an appropriate means by which to initiate our investigation of the DSMF model. Deductive reasoning does not approximate most instances of everyday reasoning as is as it explicitly provides both the premises and the conclusions that are to be assessed for validity (Mujica-Parodi et al., 2001). Real world reasoning may actually have more in common with inductive reasoning, where the premise only provides limited grounds for accepting the conclusion, and judgments of plausibility require access to background knowledge about the world (Goel & Dolan, 2004). Generally speaking, inductive arguments may better approximate the open-ended, exploratory nature of everyday reasoning (Mujica-Parodi et al., 2001). However, as evidenced by the identification of the JTC bias and hypersalience of evidence-hypothesis matches effect using variations on the beads task, a paradigm need not be a proxy of everyday reasoning for it to offer insight into differences in reasoning that may be characteristic of delusions. Further, despite the differences between inductive and deductive reasoning, both activate a similar frontal-temporal system (Goel, Gold, Kapur & Houle, 1997; Goel & Dolan, 2004), and even deductive reasoning may be significantly influenced by personal beliefs about the world, as demonstrated by the belief-bias effect. By utilising a deductive reasoning paradigm we were not seeking to identify deficits in deductive reasoning per se, but rather to use the belief-bias effect to ask the question central to the DSMF model: Why does the conflict between logic and personal beliefs not result in belief re-evaluation in delusions? Deductive reasoning paradigms allow this question to be addressed by manipulating the concordance between the logical validity of a statement and the believability of its conclusion.

A drawback of deductive and conditional reasoning paradigms is that they are cognitively demanding, and given the wide-ranging cognitive deficits associated with schizophrenia, the current paradigm should not be viewed as the only means for probing the DSMF model. Converging support should be sought using other paradigms, and in particular, paradigms that have lower cognitive demands. For example, the Stroop task (Stroop, 1935), which induces a conflict between colour naming and word reading (an automatic, habitual response), has shown a greater interference effect for people diagnosed with schizophrenia compared to healthy controls (e.g., Abramczyk, Jordan & Hegel, 1983; Carter, Robertson, Nordahl, O'Shora-Celaya & Chaderjian, 1993; Albus et al., 1996; Brebion, Smith, Gorman & Amador, 1996; Hanes, Andrews, Smith & Pantelis, 1996; McGrath, Scheldt, Welham & Clair, 1997), with brain imaging research indicating the ACC and frontal lobes as associated with Stroop task execution (e.g., Bench et al., 1993; Carter et al., 2001; Ruff, Woodward, Laurens & Liddle, 2001; Kerns, Cohen, MacDonald, Johnson, Stenger, Aizenstein & Carter, 2005).

The emotional Stroop task has been utilized to study persecutory delusions (Bentall & Kaney, 1989). In this variant of the Stroop paradigm participants may be required to name the colour of words associated with threat, depression-related words, neutral words, or meaningless letter strings. Compared to neutral words, participants with persecutory delusions respond more slowly to threat-related words, indicating the greater attendance to and task interference of words emotionally congruent with the content of their delusions. One recent functional imaging study employed a modified emotional Stroop task, overlaying emotional words on a semantically related emotional picture, and requiring participants to indicate the valence of the word, which was either congruent or incongruent with the picture (Park, Park, Chun, Kim & Kim, 2008). For emotionally incongruent stimuli the schizophrenia group was significantly less efficient (correct response rate divided by correct response time) than healthy controls and deactivated the VMPFC and subgenual cingulate gyrus significantly less. The degree of deactivation in these areas was inversely correlated with emotional interference, suggesting that a failure to inhibit automatically retrieved, task irrelevant emotional responses may have interfered with task performance in the schizophrenia group. Park et al. interpreted this data as suggesting "inefficient top-down control and deficient inhibition of bottom-up processing in the cognitive modulation over emotional processing" in schizophrenia. This explanation of schizophrenia group performance in response to incongruent emotional stimuli is consistent with the proposed dual-stream imbalance in schizophrenia suggested by the DSMF model, which indicates CMF and/or AEM as responsible for the aberrations in top-down control and bottom-up inhibition.

With early support for conflict modulation and CMF, preliminary support for emotional modulation, and the possibility that future research will provide useful information on the proposed AEM deficit, it is appropriate to consider whether there are potential clinical implications of DSMF research. A metacognitive training (MCT; Moritz, Woodward & Metacognition Study Group, 2007; Moritz & Woodward, 2007) program may provide an appropriate vehicle by which to incorporate DSMF into treatment. MCT is predicated on evidence that there are cognitive biases in schizophrenia that may contribute to psychosis, and that patients are not consciously aware of these biases. The aim of MCT is to increase patients' awareness of these biases, and how they may be responsible for fallibilities in reasoning, so that training can be provided to overcome these biases. This may reduce the severity of current symptoms and the likelihood of relapse. A similar approach may be fruitful with regards to DSMF, with the aim to increase awareness of the two streams of reasoning, and their strengths and weaknesses in different decision-making situations. Ultimately, this approach would focus on raising consciousness of the role that cognitive conflict and emotional salience may have in modulating the degree to which each stream is engaged, and the faulty reasoning that may be more likely when aberrations in these modulators occur (i.e., CMF and AEM).

7.5 Conclusion

The cognitive bias literature on delusions has been very successful at characterizing behaviours that may contribute to the formation and maintenance of delusions in schizophrenia. However, there have been few attempts to link the expression of these cognitive biases to underlying mechanisms or to generate more general models that can account for both delusion formation and maintenance. DSMF goes beyond characterizing response patterns that may be commonly observed in people with delusions, to providing a general model of delusions with mechanisms that can account for how erroneous, personally salient explanations can be accepted despite weak support and why, once formed, delusions are relatively resistant to contradictory evidence. It is the only explicitly dual-stream model of delusions to date, and the only model that explicitly frames delusions as a general decision-making process gone awry. In this context, delusions can be understood as an ongoing aberration in decision-making where decisions are made to accept and then continue to endorse an erroneous belief despite continuous presentation with belief inconsistent information, which must be ignored or adapted for delusions to be maintained.

The strength of the DSMF model is that it provides a cognitive mechanism that can account for response patterns that may be associated with delusions. However, other levels of explanation are also needed in combination with DSMF for a complete picture of the emergence and persistence of delusional beliefs. For example, the neurotransmitter approach described by Kapur's aberrant salience hypothesis, which posits a role for dysregulated dopamine transmission in psychosis, or, disconnection theories of schizophrenia such as Andreassen's Cognitive Dysmetria theory (Andreassen et al., 1996; Andreassen, Paradiso & O'Leary, 1998) and Friston's (1998) disconnection hypothesis, which offer insight into how disrupted communication between regions of the brain may contribute to the symptoms of schizophrenia. What all these models indicate is the importance of identifying the underlying processes that may be responsible for the symptoms of schizophrenia.

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Appendix I: The "bias against disconfirmatory evidence" task

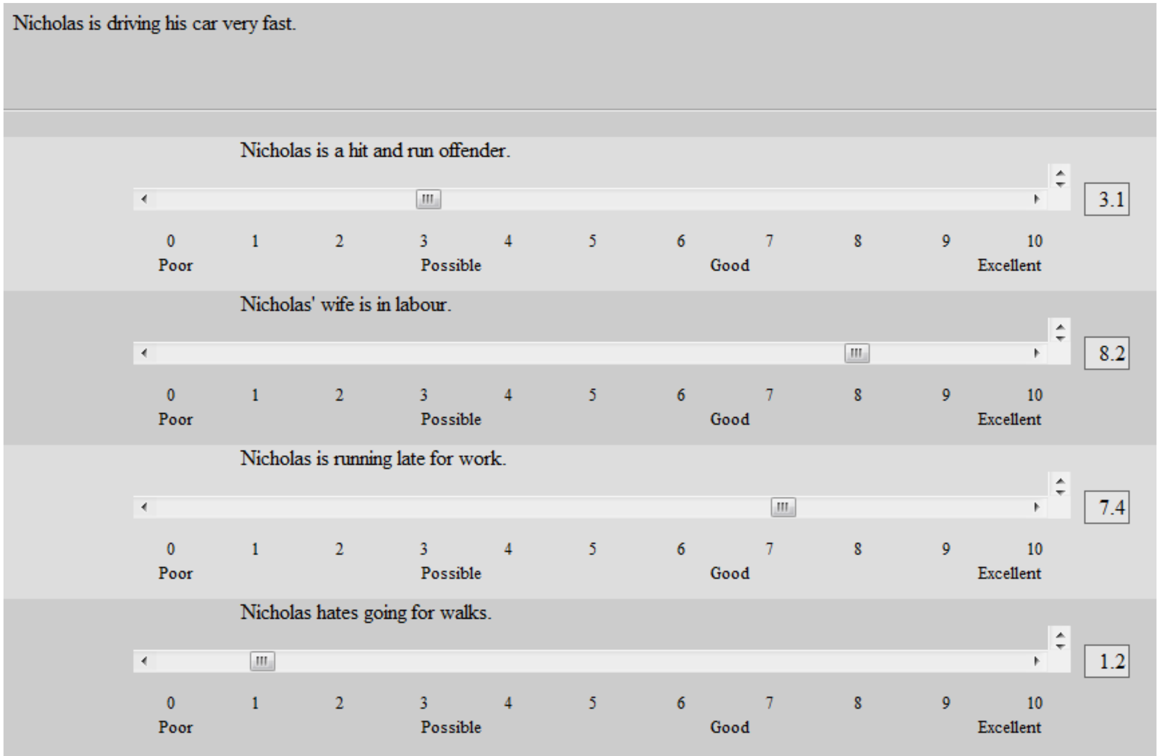

Figure A1.1 BADE screen shot 1. First scenario statement, first set of ratings.

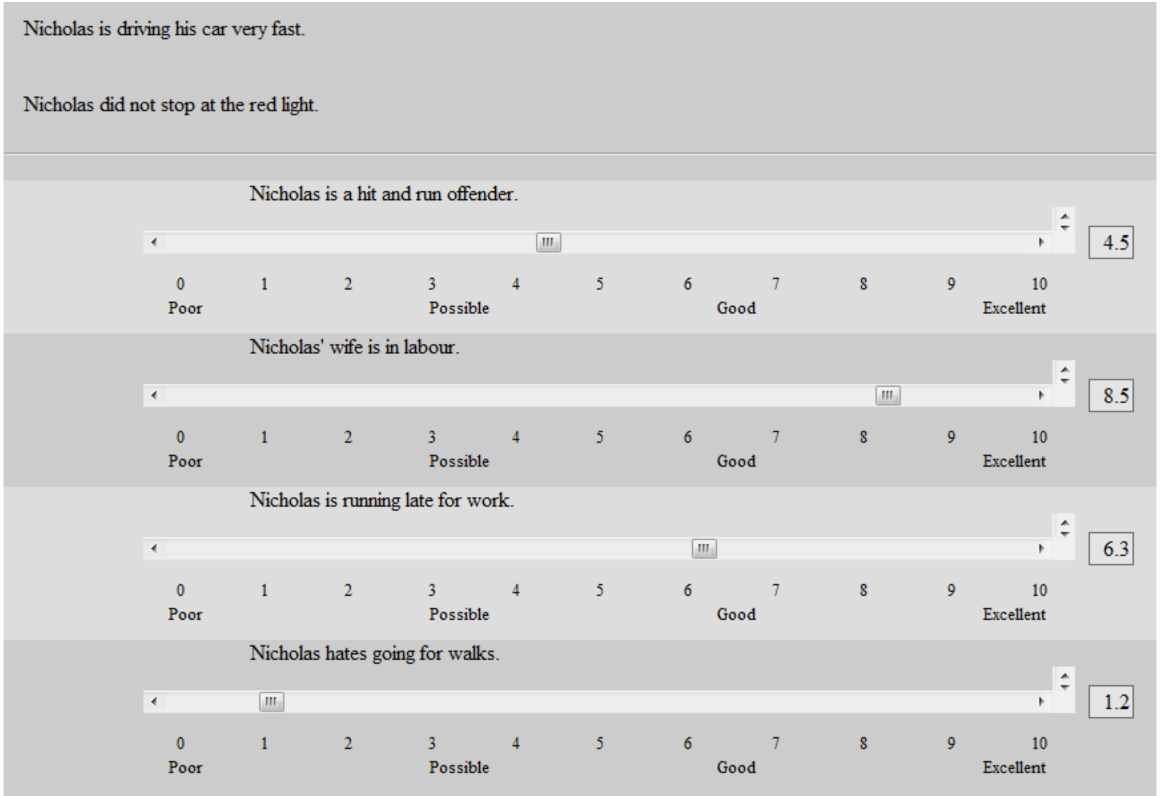

Figure A1.2 BADE screen shot 2. Second scenario statement, second set of ratings.

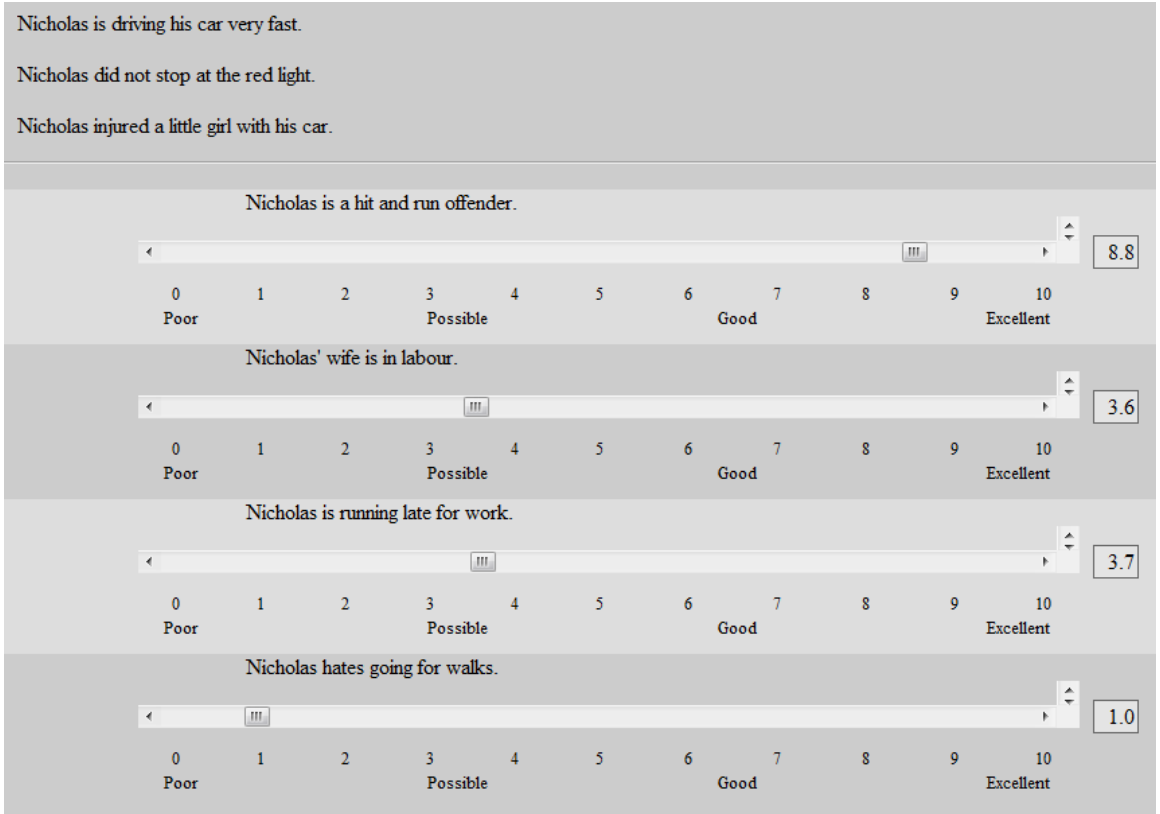

Figure A1.3 BADE screen shot 3. Third scenario statement, third set of ratings.

Appendix II: The variant "jumping-to-conclusions" task

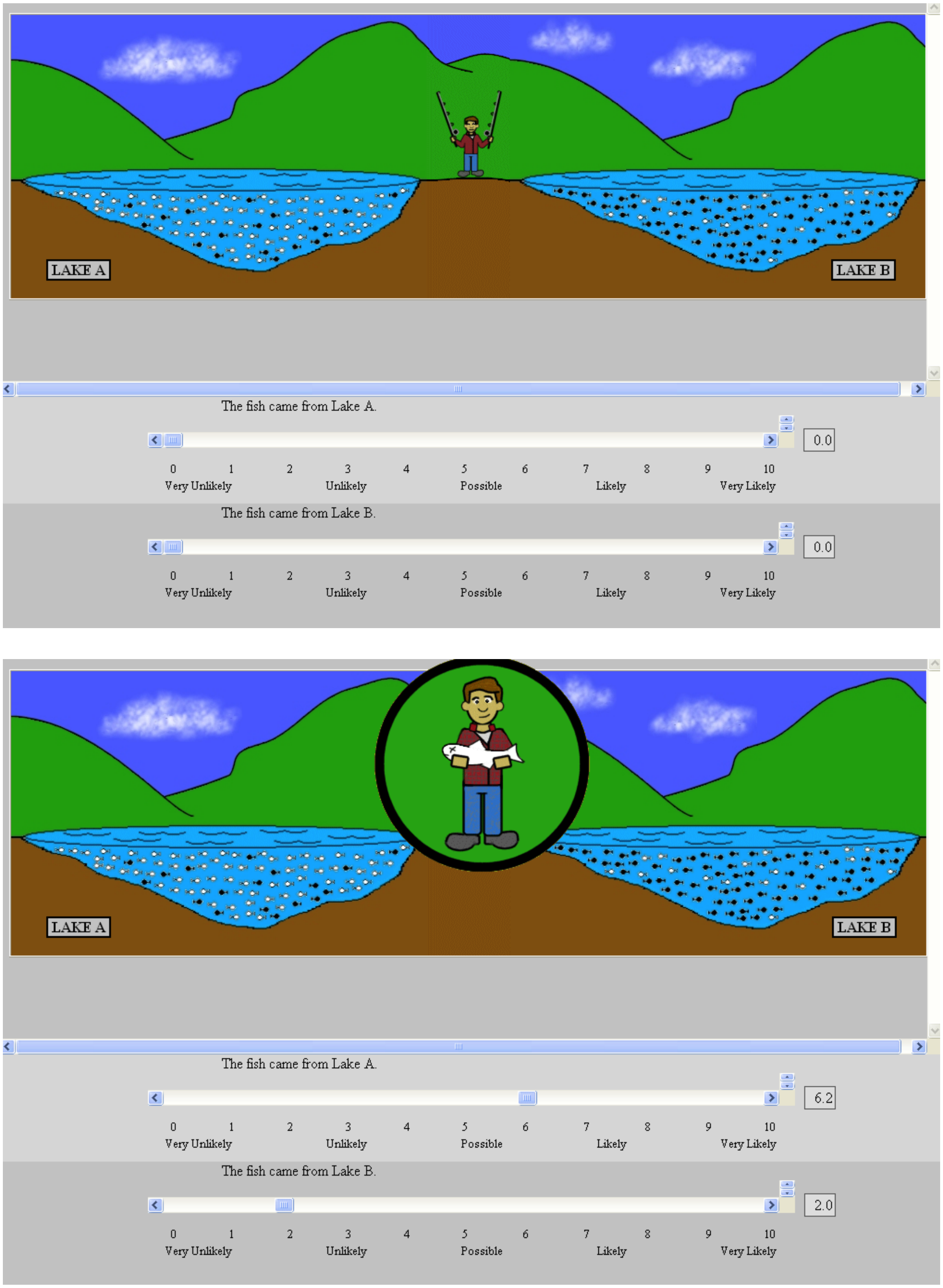

Figure A2.1 Screen shots of the variant beads task.

Appendix III: Two-part conditional stimuli from Chapter Five

Non-conflict stimuli

If some curious people are children
Then, children are never curious

If all cars run on gasoline
Then, some cars run on water

If all wheels are round
Then, some round things are wheels

If some rooted plants are trees
Then, some trees have roots

If all fish have bones
Then, some fish have bones

If bicycles always have two wheels
Then, bicycles never have three wheels

If some risk takers are gamblers
Then, gamblers never take risks

If some laws are necessary
Then, all laws are unnecessary

If bicycles always have two wheels
Then, bicycles sometimes have three wheels

If some athletes are competitive
Then, all athletes are noncompetitive

If all cigarettes are addictive
Then, some addictive things are cigarettes

If some curious people are children
Then, some children are curious

If creative people are sometimes artists
Then, some artists are creative

If all wheels are round
Then, round things are never wheels

If all cows eat grass
Then, no grass-eaters are cows

If all lions eat meat
Then, meat-eaters are never lions

If some creative people are artists
Then, artists are never creative

If all dogs bark
Then, some barking animals are dogs

If tires are made of rubber
Then, rubber is used to make tires

If all vegetables are nutritious
Then, some vegetables are unhealthy

If all trees have roots
Then, rooted plants are never trees

If all dogs bark
Then, barking animals are never dogs

If all cows eat grass
Then, some grass-eaters are cows

If some risk takers are gamblers
Then, some gamblers take risks

If all cars run on gasoline
Then, cars never run on water

If people who have been in jail are convicts
Then, all convicts have been in jail

Conflict stimuli

If cows only eat fish
Then, some cows eat grass

If lions only eat vegetables
Then, all lions eat meat

If all vegetables are unhealthy
Then, no vegetables are nutritious

If all dogs talk
Then, some talking creatures are dogs

If all vegetables are unhealthy
Then, some vegetables are nutritious

If rooted plants are never trees
Then, some trees have roots

If barking creatures are never dogs
Then, all dogs bark

If all fish are boneless
Then, some fish have bones

If cows only eat fish
Then, cows never eat grass

If bees only live in ponds
Then, bees never live in hives

If convicts have never been jailed
Then, people in jail are not convicts

If bees only live in ponds
Then, some bees live in hives

If curious people are never children
Then, some children are curious

If trees have wings
Then, some winged things are trees

If fish do not have bones
Then, all fish are boneless

If gamblers never take risks
Then, no risk takers are gamblers

If all athletes are noncompetitive
Then, no athletes are competitive

If all wheels are square
Then, some round things are wheels

If all laws are unnecessary,
Then, some laws are necessary

If all bicycles have three wheels
Then, some bicycles have two wheels

If all athletes are noncompetitive
Then, some athletes are competitive

If tires are always made of glass
Then, some tires are made of rubber

If lions only eat vegetables
Then, lions never eat meat

If children are never curious
Then, no curious people are children

If creative people are never artists
Then, no artists are creative

If some toasters are run on moonlight
Then, the moon powers some toasters

Appendix IV: Two-part conditional stimuli from Chapter Six

<u>Neutral non-conflict stimuli</u>

If all nutritious foods are vegetables
Then, some vegetables are nutritious

If all females are mothers
Then, no mothers are female

If no flying creatures are pigs
Then, no pigs can fly

If some fish are sharks
Then, no sharks are fish

If some teenagers are drivers
Then, some drivers are teenagers

If some athletes are soccer players
Then, some soccer players are athletes

If some addictive things are cigarettes
Then, no cigarettes are addictive

If no men are construction workers
Then, all construction workers are men

If some human beings are people
Then, no people are human beings

If all males are fathers
Then, no fathers are male

If some men are swimmers
Then, some swimmers are men

If no women are bank-tellers
Then, all bank-tellers are women

If all old things are antiques
Then, some antiques are old

If no meat-eaters are vegan
Then, no vegans eat meat

If all curious people are children
Then, some children are curious

If no square objects are wheels
Then, no wheels are square

If some risk-takers are gamblers
Then, some gamblers take risks

If all friendly creatures are dogs
Then, no dogs are friendly

If some meat-eaters are lions
Then, no lions eat meat

If all dangerous animals are grizzly bears
Then, no grizzly bears are dangerous

Neutral conflict stimuli

If no nutritious foods are vegetables
Then, some vegetables are nutritious

If no females are mothers
Then, some mothers are not female

If some flying creatures are pigs
Then, no pigs can fly

If no fish are sharks
Then, no sharks are fish

If no teenagers are drivers
Then, some drivers are teenagers

If no athletes are soccer players
Then, no soccer players are athletes

If no addictive things are cigarettes
Then, no cigarettes are addictive

If no men are construction workers
Then, some construction workers are men

If no human beings are people
Then, no people are human beings

If no males are fathers
Then, no fathers are male

If no men are swimmers
Then, some swimmers are men

If no women are bank-tellers
Then, some bank-tellers are women

If no old things are antiques
Then, no antiques are old

If some meat-eaters are vegan
Then, no vegans eat meat

If no curious people are children
Then, some children are curious

If some square objects are wheels
Then, no wheels are square

If no risk-takers are gamblers
Then, no gamblers take risks

If no friendly creatures are dogs
Then, some dogs are friendly

If no meat-eaters are lions
Then, no lions eat meat

If no dangerous animals are grizzly bears
Then, no grizzly bears are dangerous

Affective non-conflict stimuli

If some criminals are rapists
Then, no rapists are criminals

If no good drivers are drunk
Then, no drunk people are good drivers

If no art is child pornography
Then, no child pornography is art

If no child abuse is reduced by child porn
Then, no child porn reduces child abuse

If some welfare cheats are immigrants
Then, some immigrants are welfare cheats

If all illnesses are addictions
Then, no addictions are illnesses

If some food that tastes bad is healthy
Then, some healthy food tastes bad

If some child molesters are Catholic priests
Then, no Catholic priests are child molesters

If all women are exploited by pornography
Then, no pornography exploits women

If some stupid people are blue collar workers
Then, some blue-collar workers are stupid

If no spanking improves children's behaviour
Then, all children's behaviour is improved by spanking

If all good friends are self-centred
Then, some self-centred people make good friends

If some lazy people are unemployed
Then, no unemployed people are lazy

If all rude people are teenagers
Then, no teenagers are rude people

If all potential rapists are men
Then, some men are potential rapists

If some reckless people die young
Then, no people who die young are reckless

If some insecure people are jealous
Then, some jealous people are insecure

If all useful individuals are disabled
Then, no disabled people are useful individuals

If no childcare duties are neglected by working Moms
Then, all working Moms neglect childcare duties

If all gluttons are fat people
Then, some fat people are gluttons

Affective conflict stimuli

If no criminals are rapists
Then, some rapists are not criminals

If some good drivers are drunk
Then, no drunk people are good drivers

If some art is child pornography
Then, no child pornography is art

If some child abuse is reduced by child porn
Then, no child porn reduces child abuse

If no welfare cheats are immigrants
Then, some immigrants are welfare cheats

If no illnesses are addictions
Then, no addictions are illnesses

If no food that tastes bad is healthy
Then, some healthy food tastes bad

If no child molesters are Catholic priests
Then, no Catholic priests are child molesters

If no women are exploited by pornography
Then, no pornography exploits women

If no stupid people are blue-collar workers
Then, some blue-collar workers are stupid

If no spanking improves children's behaviour
Then, some children's behaviour is improved by spanking

If no good friends are self-centred
Then, some self-centred people make good friends

If no lazy people are unemployed
Then, no unemployed people are lazy

If no rude people are teenagers
Then, no teenagers are rude people

If no potential rapists are men
Then, no men are potential rapists

If no reckless people die young
Then, no people who die young are reckless

If no insecure people are jealous
Then, no jealous people are insecure

If no useful individuals are disabled
Then, no disabled people are useful individuals

If no childcare duties are neglected by working Moms
Then, some working Moms neglect childcare duties

If no gluttons are fat people
Then, some fat people are gluttons

Appendix V: An fMRI contrast of affective conflict vs. neutral conflict stimuli

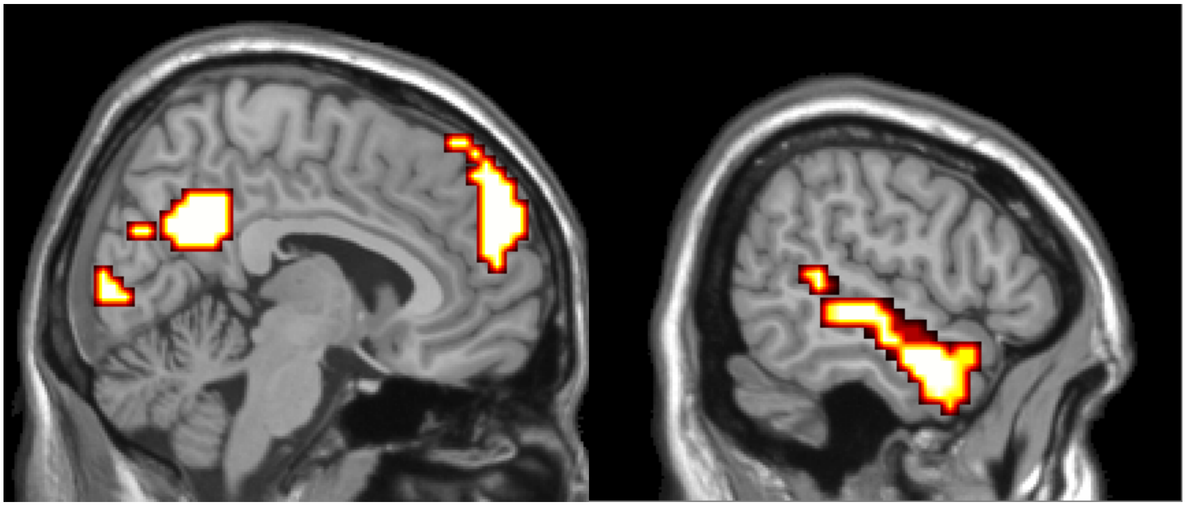

Figure A5.1 Significant activations for the "affective minus neutral" contrast.

Table A5.1 Localisation of activations for the "affective minus neutral" contrast.

Cluster Name	Peak MNI Coordinates (x, y, z)	Voxels	t =	*p* =
Lingual	-12, -84, -4	182	8.83	0.000
Mid Temporal Pole	-52, 12, -24	202	7.05	0.000
Medial Superior Frontal	-4, 56, 40	127	5.39	0.002
Calcarine	16, -88, 0	67	5.02	0.045
Precuneus	-4, -56, 28	98	4.60	0.007

Appendix VI: Task related "deactivation" data from Chapter Six

Task related deactivations

Performance of the conditional sentence task significantly deactivated a network of 340 voxels, including a VMPFC cluster and a precuneus cluster (Table A6.1; Figure A6.1). The 2x2x2 (group by salience by conflict status) ANOVA of mean beta estimates (time bins four through six) showed a significant main effect of salience, with affective stimuli deactivated less than neutral (Neutral = -0.033 (SD = 0.014), Affective = -0.028 (SD = 0.014); ($F_{1,160}$) = 5.6, $p < 0.05$), and a significant interaction of group with conflict status (($F_{1,160}$) = 3.94, $p < 0.05$). There was also a trend towards significance for the main effect of group, with less deactivation for the schizophrenia group than the control group (Healthy Controls = -0.032 (SD = 0.013), Schizophrenia = -0.028 (SD = 0.015); ($F_{1,160}$) = 3.64, p = 0.058).

Within-group t-tests showed that both the healthy control group (Neutral = -0.035 (SD = 0.011), Affective = 0.03 (SD = 0.011); t(21) = 3.23, $p < 0.01$) and the schizophrenia group (Neutral = -0.031 (SD = 0.012), Affective = 0.026 (SD = 0.012); t(21) = 2.13, $p < 0.05$) showed significantly less deactivation for affective compared to neutral stimuli. The schizophrenia group showed significantly greater deactivation for conflict stimuli compared to non-conflict stimuli (Non-Conflict = -0.025 (SD = 0.015), Conflict = -0.031 (SD = 0.012); t(21) = -1.81, $p < 0.05$), with no difference between these conditions for healthy controls (Non-Conflict = -0.034 (SD = 0.011), Conflict = -0.031 (SD = 0.011); t(21) = -1.81, p = 0.103).

Between-group t-tests showed that the healthy control group had greater deactivation for non-conflict stimuli than the schizophrenia group (t(40) = -2.04, $p < 0.05$), with no difference between groups for conflict stimuli (t(40) = 0.46, p = 0.465). There was no significant difference between groups for neutral (t(40) = -1.34, p = 0.094) or affective (t(40) = -0.92, p = 0.183) stimuli.

Table A6.1 Localisation of deactivations for task related deactivation clusters (voxels showing significant activity (t = 7.94, p = 0.00001, family wise error (FWE) correction for multiple comparisons), irrespective of group, and across both conditions).

Cluster Name	Peak MNI Coordinates (x, y, z)	Voxels	t =	*p* =
Ventromedial Prefrontal Cortex	4, 48, -8	268	18.09	0.000
Precuneus	4, -56, 20	62	10.05	0.000
Fusiform Gyrus	-32, -44, -8	4	8.72	0.000
Dorsolateral Prefrontal Cortex	-20, 32, 44	3	8.5	0.000
Ventral Posterior Cingulate Cortex	4, -28, 44	3	8.45	0.000

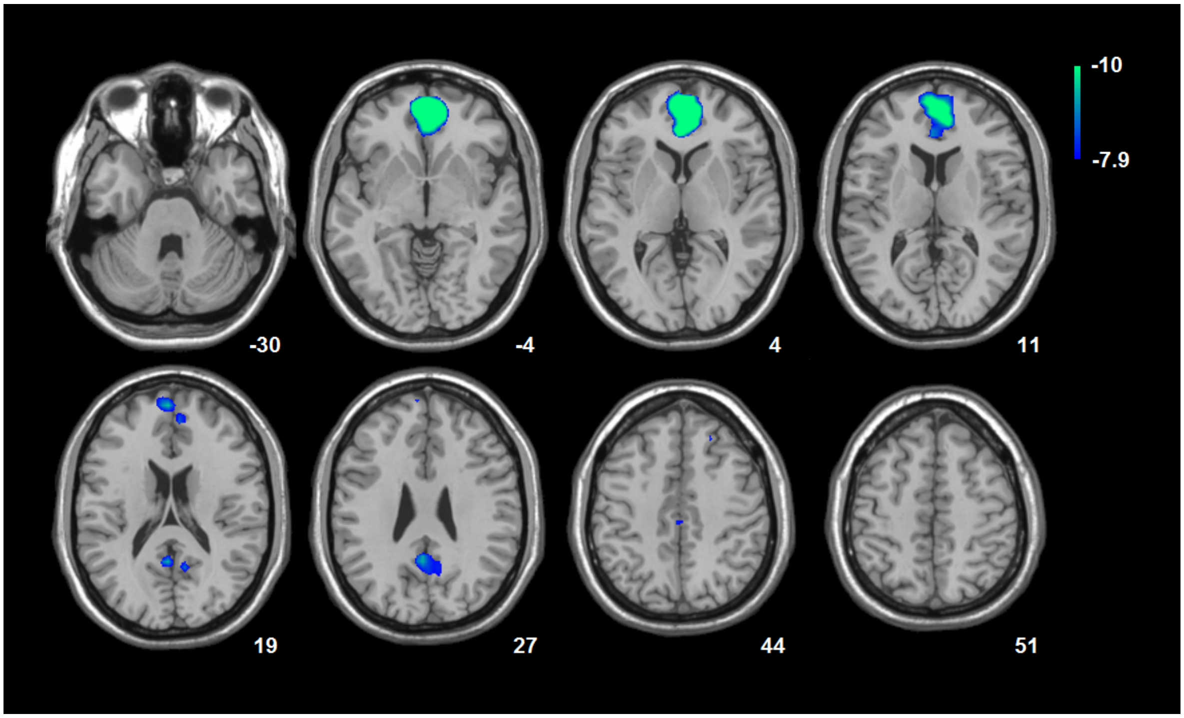

Figure A6.1 Mask of task related deactivation (corrected t = 7.94, $p = 0.00001$). This indicates significant voxels for time bins four through six from the FIR basis set, across all conditions, and irrespective of group membership.