Examining neuroanatomical correlates of switch behaviour

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Abstract

In a binary choice task, switching refers to whether an individual will switch from a previously selected option to the alternative option. Previous research within the field of decision making has shown that the outcome of a previous decision may heavily affect future decision-making strategies. Building on previous research investigating switching behaviour (Sun et al., 2018), the current study investigated the relationship rewards and punishments have on subsequent decision-making strategies within a switching task. Moreover, the current study utilised VBM (Voxel-Based Morphometry) to identify the neuroanatomical correlates of switching behaviour on a large cohort of healthy individuals (*N* = 851) taken from the Human Connectome Project. Switching was measured using an adapted reward paradigm, originally developed by (Delgado et al., 2000), whereby an individual was asked to choose whether a card was higher or lower than 5 on each trial. The results indicate increased frequency of switches after punishment which correlated negatively with grey matter volumes within the Left Superior Temporal Gyrus, Left Lingual Gyrus, Left Superior Occipital Gyrus, Right Insula, Right Medial Temporal Gyrus and left Parahippocampal Gyrus. No morphometric correlates were identified in relation to switches after rewards. Furthermore, comparing our results with 14371 fMRI studies on Neurosynth, meta-analytic co-activation revealed correlations amongst the areas identified within the structural analysis, ultimately showing increased involvement of the Insula. These findings indicate the outcome of a previous trial may directly influence the decision to switch, highlighting the potential of this study to further improve our understanding of the relationship between individual differences in both brain structure and decision making on healthy individuals.

Declaration

I declare that this is my own work, conducted during my time at University of Huddersfield for my Masters by Research Thesis. I further declare all sources of information have been correctly referenced.

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Abbreviations

OFC – Orbitofrontal Cortex

vmPFC – Ventromedial Prefrontal Cortex

LPFC – Lateral Prefrontal Cortex

VBM- Voxel based morphometry

fMRI – Functional Magnetic Resonance Imaging

PET – Positron Emission Topography

tDCS – Transcranial Direct Current Stimulation

SPM12 – Statistical Parametric Mapping Version 12

IGT – Iowa Gambling Task

HCP – Human Connectome Project

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Introduction

Throughout life we are bombarded by decisions that will require us to choose between two courses of action, the outcome of which, is often uncertain. The ability to make advantageous decisions in the face of uncertain outcomes is a required skill for survival. For example, booking a doctor's appointment may result in the detection of a problem, or it may result in long waiting times, only to be told you are in good health. According to subjective utility theory (Manktelow et al., 2012), in cases of uncertain decision making, people will weigh up the subjective probability of a certain outcome (the probability there is something medically wrong) against its subjective expected utility (early detection of illness, peace of mind etc). During these types of decisions, one must evaluate the future benefit versus previous experience. If these match, then the logical inference is that a certain decision making strategy may be optimal for survival, if not, then an alternative course of action may be required. By contrast, results found by previous studies suggest decision making may be informed by the outcome of preceding decision, which then updates an individuals subsequent decision making strategy (Xue, Lu, Levin & Bechara, 2010), consequently, they focus less on the overall outcome of a series of decisions (Ma, Zang, Cheung & Chan, 2015). This thought process is known as adaptive decision making (Sun et al., 2018).

Adaptive decision making suggests that based on previous experiences, people will often adapt and change their decision-making strategies in order to elicit more beneficial outcomes (Christakou, Brammer, Giampietro & Rubia, 2009). One of the factors that influences decision making is perspective value. When an individual makes a decision, they will assign value to the decision, dependant on the nature of the outcome. If an outcome is positive, they are more likely to pursue similar decision making strategies in the future. However, if the outcome is negative, they are less likely to pursue similar decision making strategies. Behavioural Theory (Dreher & Tremblay, 2017) suggests that rewards in general, following a decision strategy, illicit a positive response meaning the individual is more likely to pursue similar behavioural tactics that allowed them to receive rewards, providing the behaviour with positive value. For example, if an individual went to the doctors with an ailment, and received a correct diagnosis leading to the treatment of an ailment, then the behaviour of going to visit that doctor is assigned with a positive value. Inversely, if an individual is punished for making a decision, they are more likely to avoid the behaviour that resulted in a punishment or a loss, therefore the behaviour is valued as negative (Dreher & Tremblay, 2017). For example, if an individual went to the doctors with an ailment, and is misdiagnosed which led to the ailment getting worse, then the behaviour of going to visit that doctor is assigned with a negative value as it is seen as detrimental to the individual's health and survival.

Dreher and Tremblay's (2017) Behavioural Theory posits that when an individual is presented with a consequence of a decision (positive or negative), this will inform future decision making within a similar context. How an individual views a positive or negative consequence of a decision is subject to individual differences, which consequently can lead to illogical decision making strategies. Prospect Theory, developed by Kahneman and Tversky (1979), suggested an individual's view of a circumstance is limited based on the information available at that given point, leading to decision making that may be less logical and consistent. Kahneman and Tversky's (1979) model provided an explanation for individual differences in decision making as it suggested that individuals are more averse to losses than they are to potential gains. Thus, Prospect Theory posited**,** individuals are more likely to focus on losses rather than potential gains. Furthermore, the model suggests that an individual will make a decision, based on both the utility of the decision (probability of outcome and time outcome will occur) and a reference point (what the decision maker currently has) which will lead to individual differences in decision making due to these factors. For example, if a wealthy man is given the option to make a large bet with a high probability of a rewarding outcome or to not take the bet, according to Prospect Theory, they are more likely to proceed with the decision to bet. Inversely, if a poor man is given the option to make a large bet, with a high probability of a rewarding outcome, according to Prospect Theory, they are less likely to proceed with the decision to bet as the risk of losing would impact them more. Due to these reasons, Prospect Theory highlights the importance of investigating individual differences in decision making relating to reward and loss processing.

The current study aims to investigate the individual differences of reward and loss processing by investigating anatomical differences within brain structure that underlie decision making, and how this is influenced by prior outcomes. Understanding individual differences in brain structure is important to identify how neural underpinnings can influence subsequent cognitions, actions and behavioural outcomes (Finn et al., 2017). Moreover, from a scientific standpoint, it is important to correlate brain structure and function associated with behaviours in order to identify biomarkers of the behaviour that can be applied within real world contexts (Finn et al., 2017). Moreover, there is a clear need to better understand the neural correlates of behaviours due to the various problems that can arise due to maladaptive decision making (Finn et al., 2017) . For example, structural differences within brain regions have shown to be associated with; alcohol addictions (Van Holst et al., 2012), gambling addictions (Jousta et al., 2011) and internet addictions (Zhou et al., 2011). In order to better understand the neural underpinnings of certain behaviours, neuroimaging methods such as; Functional Magnetic Resonance Imaging (fMRI), Positron Emission Topography (PET) and

Voxel-Based Morphometry (VBM) have been used, alongside behavioural tasks measuring performance.

Much of the research employing the use of neuroimaging techniques such as PET (Elliott ,Frith & Dolan, 1997; Pappata et al., 2002) and fMRI (Delgado et al., 2000; McClure, Berns & Montague, 2003; O'Doherty et al., 2003; Klein-Flügge et al., 2011) have identified that rewards (i.e: the sense of a win) activate mesolimbic reward pathways associated with the dopaminergic system (Delgado et al., 2000; McClure, Berns & Montague, 2003; O'Doherty et al., 2003) and that losses activate regions of the brain associated with emotional and visceral processing such as the Insula (Krawitz, Fukunaga & Brown, 2010; Xue, Lu, Levin & Bechara, 2010) and Amygdala (Xue, Lu, Levin & Bechara, 2011). Moreover, research investigating individual differences in decision making have highlighted, the way in which an individual processes a loss may be a contributing factor into the development of addictive behaviours. Campbell-Meiklejohn, Woolrich, Passingham & Rogers (2008) conducted a study to investigate whether individuals would chase a loss (continue with the current strategy despite encountering a series of losses) or retire from the task (stop chasing the loss). They found decisions to retire were associated with increased activation in the Dorsal Anterior Cingulate Cortex, Left Anterior Insula, Posterior Cingulate Gyrus, Thalamus and Bilateral Parietal Gyrus. Moreover, individuals who decided not to chase losses showed reduced activation in the Ventromedial Prefrontal Cortex (vmPFC) and Subgenual Anterior Cingulate Cortex. Inversely they found individuals who decided to chase losses showed increased activation in the vmPFC and Subgenual Anterior Cingulate Cortex. They suggested that excessive loss chasing may be involved in the development of addictive behaviours due to a dysfunction of mesolimbic reward pathways associated with the vmPFC and Subgenual Anterior Cingulate Cortex, a similarity also seen in individuals with addictions (Qiu et al., 2014).

Prior investigations have suggested that aberrant decision making (such as loss chasing) may be a core component underlying the development of addictive behaviours. (Bechara, 2005; Diekhof, Falkai & Gruber, 2008). Initially, neurostructural studies utilising Voxel-Based Morphometry (VBM) have attempted to understand the structural underpinnings underlying aberrant decision making by investigating the relationship between brain structure in healthy participants in comparison to addicted populations. These studies are disparate in their findings, with some studies showing significant differences in brain structure between these populations (Rahman, Xu, & Potenza, 2014; Grant, Odlaug, & Chamberlain, 2015; Koehler et al., 2015; Zois et al., 2017; Ruiz de Lara et al., 2018) and others showing no differences (Joutsa et al., 2011; Van Holst et al., 2012; see section 2.1). Subsequent task based analyses suggest that grey matter volumes may be linked with disorders of aberrant decision making such as pathological gambling (Owens et al., 2019). Thus, it is important

for subsequent investigations to identify the neural basis associated with maladaptive decision making strategies. In contrast to the numerous investigations on the structural differences between addicted populations and healthy controls, few studies have investigated the effects of individual differences in brain structure associated with reward and loss processing on healthy populations. This is surprising considering studies have shown large variabilities between specific behaviours associated with individual differences in brain structure (Kanai et al., 2011 ; Banissy et al., 2012; Lai et al., 2012 ; Gu & Kanai, 2014; Krause et al., 2014 ; Owens et al., 2017; Sun et al., 2018). Moreover, lesion studies have shown that focal damage to specific brain regions can have an impact on how an individual views an outcome (reward or loss) and their decision making thereafter (Clark et al., 2014; Weller, Levin, Shiv, & Bechara, 2007) Therefore, there exists a need to further elucidate the association between neuroanatomy and individual differences in decision making following reward or loss.

In the current study, we aimed to investigate how receipt of either a reward or a punishment influenced future decision making; whether people would stick, or switch, from one of two response options after receiving a reward or loss. In addition, the study will replicate previous research by Sun et al. (2018) which identified significant associations between neuroanatomical structure and general switching behaviour (switching regardless of preceding trial). Moreover, this thesis will aim to build on existing research (Sun et al., 2018) by investigating the associations between brain structure and switches after rewards in comparison to switches after losses on a large sample of healthy subjects. Given previous research has suggested individuals may be generally more loss averse (Kahneman & Tversky, 1979), we predict that there will be an association with grey matter volumes and increased frequency of switches following loss trials. Initially, this thesis will provide a brief review of the current literature surrounding the neuroanatomical correlates of decision making relating to reward and loss processing. Moreover, we will employ Voxel-based Morphometry (VBM) to analyse grey matter volumes and will measure switching behaviour by adapting and utilising a previously used fMRI reward paradigm (Delgado et al., 2000).

Literature review

2.1 Brain structure and maladaptive decision making

In order to identify the neural underpinnings of reward processing, a large number of previous studies have utilised fMRI. fMRI is a non-invasive brain scanning method to measure the differentiation between oxygenated and deoxygenated haemoglobin, which reflects metabolic changes in areas of the brain that are more active. Several fMRI studies have suggested that receipt of a reward recruits the Ventral Striatum, located within the Basal Ganglia, showing increased activation within this region when a reward is presented (Delgado et al., 2000; McClure, Berns & Montague, 2003; O'Doherty et al., 2003; Klein-Flügge et al., 2011; Galtress, Marshall, & Kirkpatrick, 2012; Haber & Knutson, 2010; O'Doherty et al., 2004). Given the large amount of comparative findings highlighted by fMRI studies, researchers are now moving to investigate the associations between reward processing and brain structure, in order to further investigate the involvement of these regions in reward processing.

Initially, in order to investigate whether structural differences influence decision making relating to reward processing, previous studies have assessed the relationship between anatomical brain structure within healthy individuals in comparison to individuals with addictive disorders. To investigate morphometric differences in brain structure and associations with behaviour, studies will employ Voxel-based Morphometry (VBM). VBM is a technique using structural MRI scans, that allows for voxel-wise comparison of local grey matter concentrations across individuals, using the statistical approach of parametric mapping (Ashburner & Friston, 2000; Ashburner, 2007). When investigating structural differences of problem gamblers versus healthy individuals, preliminary VBM studies have identified little evidence of differences in brain morphometry associated with these two populations. One of the first studies to use VBM in relation to problem gambling disorder was conducted by Joutsa et al. (2011). Interestingly, they found no significant differences to controls within both grey matter and white matter volumes in individuals with gambling disorders. They also conducted Diffusion Tensor Imaging in relation to white matter volumes and found that 12 problem gamblers in comparison to 12 healthy controls showed lower white matter integrity in multiple brain regions; Corpus Callosum, the Cingulum, Anterior Limb of Internal Capsule (white matter tract from Thalamus to Frontal Lobe), Anterior Thalamic Radiation, Inferior Longitudinal Fascicle (white matter tract between Temporal and Occipital Lobe; Ashtari (2012) and Inferior Fronto-Occipital Fascicle. Although no grey matter differences were identified, the study by Jousta et al. (2011) was the first to identify differences in brain structure that may be associated with gambling addiction, highlighting

how differences in brain structure may be associated with reward malfunction, which could underlie some aspects of addiction.

Van Holst et al. (2012) investigated whether grey matter atrophy within problem gamblers were neuroadaptations to increased recruitment of reward regions or whether there is a common neurobiological vulnerability for addictive behaviours that relates to brain structure. Previous research has shown that individuals who are addicted to alcohol are also more likely to perform poorly on gambling-based tasks. For example; Fein et al. (2006) investigated grey matter atrophy in relation to performance on the simulated gambling task and found individuals with alcohol use disorder (AUD) showed lower grey matter volumes within the Amygdala which correlated with poorer performance on the simulated gambling task. Further to this research Van Holst et al. (2012), investigated grey matter volumes in 36 individuals with AUD, 40 participants who were identified as problem gamblers in comparison with 54 healthy controls. Whole brain VBM analysis revealed individuals with AUD showed significant grey matter atrophy within the Right Insula Cortex, Right Putamen, Left Superior Frontal Cortex, Right Supermarginal Cortex, Left Precentral Cortex, Left Thalamus and Bilateral Superior Parietal Cortex in comparison to both problem gamblers and healthy controls. Similar to findings by Joutsa et al. (2011), there were no significant differences in grey matter volumes between problem gamblers and healthy controls. Although differences in grey matter volumes found within Van Holst et al. (2012) study could be due to toxic effects of alcohol, it is a significant finding as it shows individuals with maladaptive reward related behavioural strategies may be associated with structural differences, prompting studies to further investigate the relationship between brain structure and behaviour. Consequently, future studies investigating structural differences between problem gamblers and healthy controls, have yielded significant findings (Rahman, Xu, & Potenza, 2014; Grant, Odlaug, & Chamberlain, 2015; Koehler et al., 2015; Zois et al., 2017; Ruiz de Lara et al., 2018; see Table 1 for summary of VBM literature.), showing grey matter differences within both frontal and reward regions of the brain.

VBM studies investigating structural correlates of addictions such as; internet addiction in conjunction with online gaming (Han, Lyoo, & Renshaw, 2012); general internet addictions (Hong et al., 2013) and video game addictions (Kühn et al., 2011) have found associations between grey matter volumes and behavioural addictions, again showing that maladaptive decision making strategies show a relationship with structural differences. In relation to internet addictions, VBM studies found that individuals with internet addictions had lower grey matter volumes within the Right Orbitofrontal Cortex (Hong et al., 2013) and lower grey matter volumes within Left Anterior Cingulate Cortex, Left Insula, Left Posterior Cingulate Cortex, and Left Lingual Gyrus (Zhou et al., 2011). These results and the results identified above, highlight structural differences in regions

associated with reward processing, emotion and executive function, providing further evidence of the relationship between brain structure and maladaptive decision making.

Studies using VBM have also been conducted to investigate the relationship between structural differences among other clinical populations in relation to reward and loss processing. Moreno-López et al. (2012) conducted a study assessing neuroanatomical correlates of impulsivity and reward sensitivity in adolescents with excessive weight versus healthy controls. Using a region of interest approach, they found individuals with excessive weight was associated with higher volumes of grey matter within the Right Hippocampus. Within healthy controls they also found that grey matter volumes may be associated with reward sensitivity and positive urgency, highlighting that individuals with a higher weight measurement have structural differences within areas that have been previously associated with sensory processes and motivational decision making. Other studies investigating reward processing relating to obesity (Shott et al., 2015) have shown that obese individuals tend to show lower grey matter and white matter volumes within the Orbitofrontal Cortex, Striatum and Insula in comparison to healthy controls. Moreover, they found an association between obese individuals and increased sensitivity to negative reinforcement, measured by the reward and punishment sensitivity questionnaire.

Given the increased volume of research highlighting associations between structure and addictive behaviours, Koehler et al. (2015) replicated previous studies investigating brain structure in individuals with gambling addictions, by conducting a further VBM analysis on structural MRI scans of 20 problem gamblers versus 21 healthy controls. They found that problem gamblers had increased grey matter volumes in both the Right Ventral Striatum and Right Middle Frontal Gyrus in comparison to healthy controls. Functional studies have also identified increased activation of the ventral striatum in problem gamblers in comparison to healthy controls (Linnet et al., 2010). This showed an increase in problem gambling behaviours which may also reflect in structural differences within brain regions implicated in reward processing. This highlights the importance of structural studies to constantly investigate the relationship between structural differences in the brain and decision making strategies.

Table 1. VBM studies measuring grey matter reductions within problem gamblers in comparison to healthy controls. Studies have different methodologies so are not directly comparable.

VBM studies	**Grey matter reductions in gamblers compared with healthy controls**
Joutsa et al. (2011).	No differences
Van Holst et al. (2012),	No differences
Rahman, Xu, & Potenza (2014)	Left Hippocampus, Right Amygdala
Grant, Odlaug, & Chamberlain (2015)	Right Superior Frontal Cortex, Right Middle Frontal Cortex, Right Orbitofrontal Cortex, Left Inferior parietal Lobe, Right Post-central Gyrus, Right Supermarginal Gyrus, Right Superior Frontal Gyrus
Koehler et al. (2015)	Right Ventral Striatum, Right Middle Frontal Gyrus
Zois et al. (2017)	Superior Medial Frontal Cortex, Orbitofrontal Cortex
Ruiz de Lara et al. (2018)	Dorsal Medial Prefrontal Cortex

2.2 Lesion studies and decision making

Investigations into the neuroanatomical differences between healthy individuals in comparison to individuals with addictions has highlighted some differences in brain anatomy which may be associated with maladaptive decision making strategies. Another way in which brain structure has shown to be associated with decision making ability, is through investigation of the impact brain damage has on decision making. Damasio (1994), found that individuals with damage to the ventromedial prefrontal Cortex had normal intelligence, normal neuropsychological function, and normal frontal lobe function. However, they were shown to have severe impairment in both personal and social conduct, and impairment within decision making abilities that were based on these factors. He found these individuals had difficulties with both immediate and future planning, were unable to make decisions that would be personally advantageous, and often could not maintain relationships with people and suffered social and economic losses. He concluded that deficits in these abilities and associated structures would lead to deficits within the emotional mechanism that would assess consequences of a particular action (Bechara, & Damasio, 2005). In order to investigate the processes that underlie damage to the ventromedial prefrontal Cortex, Bechara, Damasio, Damasio and Anderson (1994) developed the Iowa Gambling Task (IGT) in order to assess how individuals make decisions that would be personally advantageous based on the trade-off between immediate and future planning strategies.

The IGT is one of the most widely used paradigms to investigate decision making processes. Originally designed by Bechara, Damasio, Damasio and Anderson (1994), the task involves four virtual card decks (A, B, C & D) from which participants are instructed to choose a card from any of the four decks. Following each choice, participants are either rewarded (monetary reward) or punished (monetary loss). Participants can change decks at will, and are instructed to win as much money as they can, and to lose as little money as possible. Unknown to the participants, decks A and B are advantageous in the short term as they have higher immediate reward amounts given, however disadvantageous in the longer term due to higher punishment amounts (participants have to pay more penalties). Inversely, decks C and D are less rewarding in the short term however advantageous in the long term due to lower punishment rate, meaning participants are more likely to retain money using these decks. The optimal strategy for task completion, defined by Bechara, Damasio, Damasio and Anderson (1994), was to gradually learn the rules of the task and to select decks that benefited them in the long run rather than choosing disadvantageous decks resulting in immediate gratification. Thus, the metrics extracted from the Iowa gambling task are the sum of cards selected from the advantageous decks compared with the sum of cards selected from disadvantageous decks. In their study Bechara, Damasio, Damasio and Anderson (1994) revealed

that individuals with damage to prefrontal areas chose more cards within the disadvantageous decks in comparison to healthy controls. This initial finding provides evidence that performance in reward related tasks is related to brain structure, leading to further studies investigating how performance on tasks such as the IGT is influenced by both brain structure and function.

Overall, the purpose of the IGT is to focus on how individuals react to rewards and their ability to monitor reward frequency, in order to maximise reward amount by choosing advantageous decks leading to increased task performance (Higher amount of money won). As highlighted in a review of the Iowa gambling task by Lin, Song, Chen, Lee and Chiu (2013) the task can also be used to assess punishment frequency and can assess how this influences future decision making behaviours. Ma, Zang, Cheung and Chan (2015) aimed to investigate how punishment frequency influences brain activation on participants completing the IGT. They recruited 24 participants and instructed them to perform the original version of the IGT designed by (Bechara, Damasio, Damasio & Anderson, 1994). Using fMRI, they found that during risky decks (A & B) significantly greater activation was seen in the Right Anterior Cingulate Cortex, Right Middle Temporal Gyrus, Right Inferior Frontal Gyrus and Right Thalamus. In order to examine the impact of punishment frequency they investigated the difference in activation under high punishment frequency in comparison to low punishment frequency (comparing decks A & C to decks B & D). They found significantly greater activation within the Anterior Cingulate Cortex under high punishment frequency decks in comparison to low punishment frequency decks. When conducting further analysis, they revealed participants would change preference for card decks depending on long term outcomes, however throughout the task participants would avoid decks with high punishment frequencies. These findings build on research by Kahneman and Tversky (1979), as they provide support that individuals may be more aversive to losses and highlight the involvement of brain function which may be associated with the way in which an individual responds to a punishment

2.3 Anatomical correlates of decision making

Damasio (1994) identified the Insula Cortex to be a critical neural substrate involved within emotion-based decision making. He suggested the Insula may be involved in emotional feelings that can arise when an individual is presented with an emotionally triggering stimulus, such as a reward or loss, later measured by the Iowa gambling task (Bechara, Damasio, Damasio & Anderson, 1994; Krawitz, Fukunaga & Brown, 2010; Lin, Song, Chen, Lee & Chiu, 2013). As mentioned within numerous studies utilising the Iowa gambling task (Krawitz, Fukunaga & Brown, 2010), the somatic marker hypothesis suggests that the Insula may play an important role (Bechara, & Damasio, 2005) in emotional based

decision making by forming a circuitry system with the ventromedial prefrontal Cortex and somatosensory Cortex. Craig (2002) suggested the Insula was involved with conscious interoceptive awareness, which continually tracks the ongoing physiological processes within the body. Supportive evidence for the role of the Insula is shown within studies investigating the role of the Insula and its relationship with addictive behaviours (see review by Naqvi & Bechara, 2010). In studies investigating smoking cessation and Insula damage (Naqvi, Rudrauf, Damasio & Bechara, 2007; Naqvi & Bechara, 2010), individuals following focal damage to the Insula (Insula lesion) have stopped smoking without complications or difficulty, in comparison to individuals with other brain injuries, highlighting the role of this area in decision making relating to addictive behaviours and ultimately suggesting this area may be involved In conscious urges or cravings.

Given the Insula has been associated with the maintenance of maladaptive decisions, further studies investigating Insula damage suggest that damage to the Insula Cortex may lead to altered decision-making strategies, in comparison to healthy individuals, involving risky gains and losses. Weller, Levin, Shiv and Bechara (2009) compared risky decision-making strategies in Insula lesion patients to healthy controls using a computerised version of the cups task developed in an earlier study (Weller, Levin, Shiv, & Bechara, 2007). Modified from the original cups task developed by Levin and Hart (2003), the task consists of an array of 2, 3 or 5 cups shown on each side of the computer screen. One side of the screen was designated as 'certain', in which choosing a cup would lead to a designated win or loss amount (win or lose $0.25). The other side corresponded to a 'risky side' in which a selection of a specific cup could lead to a win or loss of a designated number of quarters ($0.25). Selection of any other cup on this side lead to a no win/no loss outcome. They found that patients with Insula damage made fewer risky decisions regardless of whether the trial was a risky reward or risky loss in comparison to healthy individuals. Differing reactions to rewards and losses following Insula damage, highlights the involvement of this area in how an individual makes decision based on potential reward or loss outcomes, and consequently provides further evidence that brain structure may influence reward related behaviours.

Insula damage has also been associated with reductions in cognitive biases within gambling tasks (Clark et al., 2014). Decision making within a gambling setting has often highlighted certain cognitive distortions that may play a role in the maintenance of maladaptive decision-making strategies. Gamblers fallacy is a cognitive bias in which the individual believes previous events influence future outcomes within a gambling setting when the probability of subsequent outcomes remains constant (Xue, Lu, Levin, & Bechara, 2011). An example of this would be a coin toss in which the probability of the coin landing on either heads or tails is 50%. Gamblers fallacy bias would lead an individual to believe that because a certain number of outcomes have been constant (i.e. landing on heads three

times) then the outcome must change even though the outcome of the next trial will always be 50% probability of landing on either heads or tails. Clark et al. (2014) investigated how lesions within the Insula affected cognitive bias within gambling tasks. Using a roulette task, they found that within healthy individuals, binary choice patterns displayed negative recency (whereby the choice of either red or black decreased due to the previous run of that colour) associated with gamblers fallacy. Inversely they found that in individuals with Insula damage presented no avoidance of recent outcomes. Moreover, when conducting a slot machine task, Clark et al. (2014) found that near miss outcomes (an outcome marginally close to a win) increased motivation to continue the game. Inversely, individuals with Insula damage showed no evidence of increased motivation. This provides compelling evidence that the Insula may be involved in managing future decision-making strategies that are dependent on previous outcomes.

Structural differences in affective and cognitive brain regions may play a role in how individuals respond to rewards compared to losses which may affect future decision making strategies. Research using the Wisconsin Card Sort Task (where participants are asked to match cards to 3 categories; shape, colour, number of designs on the face of the cards) has shown that individuals with damage to the Prefrontal Cortex tend to stick with a learned rule rather than switch to alternatives, even when presented with negative task feedback (Liu, Braunlich, Wehe & Seger, 2015). Furthermore, in a study where rewards and punishments are determined by a coin flipping task, Shiv et al. (2005) assessed risky behaviours in 20 participants who had lesions in areas associated with emotional circuitry (15 patients with lesions within Bilateral Amygdala and damage to Hippocampus, 3 patients with lesions located within the Bilateral Orbitofrontal Cortex, 8 patients with lesions in the Right Insula Cortex and 4 patients with lesions in the Somatosensory Cortex) against 19 healthy participants with the inclusion of 7 control patients with lesions in brain regions not associated with emotional processing (lesions in the Dorsolateral Prefrontal Cortex). They found that both healthy participants and control participants invested in 40.5% of rounds following losses whereas participants who had lesions in areas associated with emotional processing (Orbitofrontal Cortex Frontal Cortex, Insula Cortex and Amygdala) invested in 85.2% of rounds following losses. This research provides evidence that structural differences in brain regions may affect decision making after an individual experiences a reward or loss. It is however important to note that, although finding similar results, it is difficult to draw conclusions from brain lesion studies identified above. Damage to the brain can be caused by a variety of different factors meaning the areas in which lesions have formed provide a degree of inconsistency, as it is likely no two lesions will be exactly the same. Also, when a lesion is present, it is often unclear how the brain compensates for the damage (Rick, 2011). Therefore, it is important to conduct research investigating how structural

differences among healthy individuals correlate with behaviour. One of the methods used to analyse this is Voxel Based Morphometry which the current study uses to investigate neural anatomical correlates of switch behaviour.

2.4 Voxel-Based Morphometry

Studies investigating focal brain damage and how this impacts decision making have shown that structural damage may be associated with atypical behavioural patterns in comparison to healthy individuals. However, research investigating how brain structure in healthy individuals (individuals without lesions or addictions) influences reward and loss processing is less well understood, due to the limited number of studies, leading to further studies to investigate structural correlates of decision making on healthy individuals. One task used to measure adaptive decision making in healthy individuals, is the Delay Discounting Task. The Delay Discounting Task is designed to assess whether the participant will restrain from immediate gratification in the knowledge that if they do they will receive a larger future reward. An example of a Delay Discounting Task is the Stanford Marshmallow Experiment (Mischel, Ebbesen & Raskoff-Zeiss, 1972). In this study children were given a marshmallow and told that if they refrained from consuming the first marshmallow, they would receive another 15 minutes later. Following this initial experiment, researchers replicated the tasks on adults using monetary rewards (Kirby, Petry & Bickel, 1999) within numerous event related fMRI studies (McClure, Laibson, Loewenstein & Cohen, 2004; Ballard & Knutson, 2009; Albrecht et al., 2011; de Water et al., 2017) finding significant positive correlations between activation and future reward magnitude within the mesolimbic reward pathway (Ballard & Knutson, 2009). Following significant results in recurrent fMRI studies, researchers set out to investigate the structural correlates of choice behaviour within the Delay Discounting Task using VBM (Cho et al., 2013; Tschernegg et al., 2015; Mohammadi et al., 2016; Owens et al., 2017). One of the first studies to investigate structural correlates of delay discounting among healthy individuals, conducted by Cho et al. (2013), found grey matter volumes of the Bilateral Medial Frontal Gyrus, Bilateral Anterior Cingulate Gyrus, Left Middle Cingulate Gyrus and Right Orbitofrontal Gyrus positively correlated with discounting rates, whereas, grey matter volumes within Bilateral Ventral Putamen, negatively correlated with discounting rates. This initial study, highlighted the importance of looking at structure within healthy individuals and highlighted the importance of bringing functional and structural studies together to provide a more holistic picture, prompting future studies to also investigate similar effects.

Tschernegg et al. (2015) further investigated the relationship between brain structure in healthy individuals and performance on the Delay Discounting Task, however they found disparate results in comparison to previous research by Cho et al. (2013). Tschernegg et al. (2015) recruited 51 women and 19 men who were assessed as healthy individuals via self-report questionnaire. Each participant was given a structural MRI scan and completed the Delay Discounting Task after the scan. The VBM analysis revealed there was a significant positive correlation between discounting rates and grey matter volume within the Right Caudate, with further subcortical Freesurfer analysis revealing a positive correlation between grey matter volumes in both the Left and Right Caudate, however these were measured at an uncorrected level.

In order to consolidate the effects brain structure has on decision making in relation to rewards, a large scale VBM study, conducted by Owens et al. (2017) replicated previous VBM studies using a large open source data set; The Human Connectome Project (Van Essen et al. HCP, 2013). They found that grey matter volumes within the bilateral Middle Temporal Gyrus and Bilateral Entorhinal Cortex positively correlated with discounting rates, again showing different results from the results obtained from previous literature (Cho et al., 2013; Tschernegg et al., 2016). The disparate literature identified in previous studies highlights the importance of using large scale studies to continually investigate structural correlates and to improve understanding of how the brain processes choice between two alternatives when influenced by a reward.

An alternative way which VBM can investigate the relationship between brain structure and reward processing on a decision-making paradigm, is to compare healthy individuals to individuals with addictive disorders. Using the delayed discounting task, Mohammadi et al., (2016) investigated how both healthy participants and problem gamblers performed on an intertemporal task and how performance in this task correlated with structural volume. In order to assess this, they conducted two studies; the first study, investigating intertemporal choice on 40 healthy individuals, and the second study consisting of a group comparison examining the effects of brain structure on 15 problem gamblers versus 15 healthy individuals. Using VBM analysis, Mohammadi et al. (2016) found that within the first study, discounting rates among healthy participants positively correlated with grey matter volumes within the left Insula Cortex, superior division of Right Lateral Occipital Cortex and Right Orbitofrontal Cortex however showed a negative correlation of grey matter volumes within the Left Frontal Pole. Results from study two revealed, in comparison to healthy individuals, problem gamblers showed decreased grey matter within the Right Orbitofrontal Cortex, Right Precentral Gyrus, Right Insula, Right Amygdala, Right Hippocampus, Right Anterior Cingulate Gyrus and Bilateral Supplementary Motor Area. The results identified within the first study provide evidence that healthy individuals show individual differences in brain structure that is associated

with altered decision making strategies within a reward task. Moreover, the results from the second study provide a comparison between healthy and clinical populations, providing supportive evidence for the involvement of brain structure within individuals diagnosed with gambling additions, a maladaptive decision making disorder involving reward regions of the brain. Research by Mohammadi et al. (2016) and others highlighted above, provide evidence that structural differences are not purely identified within individuals with addictions. Structural differences can also extend to healthy individuals and may be associated with individual differences in decision making strategies, therefore it is important for research to further investigate the relationship of brain structure in healthy individuals and decision making.

2.7 Switching

Prospect Theory (Kahneman & Tversky, 1979) has highlighted that individual differences in decision making can be a result of prior outcomes and suggests that individuals will update their decision-making strategy based on prior outcomes, which can lead to illogical decision making strategies such as; The Gamblers Fallacy strategy. Xue et al. (2012) investigated how healthy individuals reacted to previous decisions and how this can lead to maladaptive decision-making strategies. Using a gamblers fallacy task, in which a participant had to choose between a red or black card over a series of repeated trials, Xue et al. (2012) identified that increased activation within the left prefrontal Cortex (LPFC) was associated with increased the use of gamblers fallacy. Moreover, using Transcranial Direct Current Stimulation (tDCS) of the LPFC increased the use of gamblers fallacy which resulted in individuals sticking with current decisions and switching within the next trial after long streaks, indicating the LPFC is strongly associated with switching frequency within a binary choice task. The use of corroboratory evidence from the combined methods of tDCS and fMRI within this study providing further evidence that prefrontal regions of the brain may also be involved in maladaptive decision making strategies.

VBM studies have also highlighted individual differences relating to sensitivity to reward or punishment outcomes. Adrián-Ventura, Costumero, Parcet & Ávila (2019) assessed reward and punishment sensitivity using The Reward and Punishment Sensitivity Questionnaire (Torrubia, Ávila, Moltó & Caseras, 2001). They found a significant positive correlation with grey matter volumes within the Amygdala and sensitivity to punishment, whereas they found a significant negative correlation between grey matter volumes within the Left Lateral Medial Prefrontal Cortex and Left Medial Prefrontal Cortex. This recent study, provides good evidence that brain structure may be associated with how an individual views either a reward or a punishment. Functional studies have

also identified associations between activation of brain regions and decision making following reward or loss outcomes. Using fMRI, Xue, Lu, Levin & Bechara (2010) investigated how the Insula was involved in future decision making based on the results from a previous choice in relation to risky decision making. They found, if an individual took a decision with less risk initially, the subsequent decision was riskier, recruiting stronger activation within the Insula. This may suggest that the Insula tracks previous outcomes that may inform future risky decision making strategies. Furthermore, a subsequent fMRI study (Xue, Lu, Levin & Bechara, 2011) investigated the effect of prior outcomes on subsequent decision making found young adults displayed increased amounts of risky decision making after losing a gamble in comparison to winning the gamble. They found risky decisions were positively correlated with increased activation in frontoparietal network and left lateral orbitofrontal Cortex, however correlated negatively with activation in the Amygdala and the Caudate Nucleus. The results from these studies further highlights how previous outcomes can affect future decision making, and provides support of the involvement of brain regions, evidenced from both functional and structural studies. Moreover, the results from this study suggest individuals are more sensitive to punishments and change their behaviour following a punishment in comparison to a reward. To our knowledge, no study has addressed how the combination of both prior outcomes and reward and punishment processing have on future decisions. The current study aims to build on previous research (Xue, Lu, Levin & Bechara, 2010; Xue, Lu, Levin & Bechara, 2011; Xue et al., 2012; Adrián-Ventura, Costumero, Parcet & Ávila, 2019) by addressing the structural correlates of reward and loss processing within a switching task. Building on the work by Sun et al. (2018), we aim to investigate how grey matter volumes are associated with increased frequency of switches following reward or punishment trials.

Sun et al. (2018) investigated repeated binary choice patterns in decision making and assessed how often an individual would stick with a specific choice or switch to an alternative, and whether this behaviour correlated with structural differences in the brain. Alongside measuring frequency of switches, Sun et al., (2018) also investigated cognitive flexibility using persistence error measured by the Wisconsin Card Sorting Task (Liu, 1999), and personality traits of persistence were measured using the Temperament and Character Inventory-Revised (Cloninger, Svrakic & Przybeck, 1993). In order to accurately measure 'switching' behaviour, they used a card guessing task in which participants were asked to match a computer-generated sequence of either a red or black card Xue, Lu, Levin & Bechara, 2010; Xue et al., 2012). They informed the participants that the computer generated sequence was random, however the programme followed a sequence to which the computer picked an equal amount of both options (50% red and 50% black) For every correct guess they would win 1 CNY (Chinese Yuans) and for every incorrect guess, they lost 1 CNY. The optimal

strategy was for participants to guess, however they found that switching rate for participants was significantly lower (43%) than the switching rate for the computer (50%) suggesting the majority of participants will stick with an option rather than switch to an alternative. Results from the VBM analysis revealed that grey matter volumes in the Posterior Cingulate Gyrus, left Insula Cortex and Frontal Pole positively correlated with card switching frequency. Moreover, they found card switching frequency negatively correlated with grey matter volumes in the Medial Temporal Lobe and Right Insula Cortex. Although providing evidence that switching behaviour is correlated with grey matter volumes in specific areas, this study did not assess how switching behaviour could be motivated by the outcome of the previous trial. The current study aims to replicate the findings from the study conducted by Sun et al. (2018) by investigating general switching on a large cohort of healthy individuals. We also aim to extend the findings of Sun et al. (2018) by investigating whether grey matter volumes relate to switching behaviour following either a win or a loss trial.

The Current study

In the literature surrounding rewards and loss processing, a number of inconsistencies arise. Studies investigating structural differences in relation to gambling tasks have been mostly either lesion studies or studies investigating structural differences in comparison to clinical populations. Therefore, it is difficult to draw conclusions in relation to brain structures involved in reward and loss processing on healthy individuals, given the limited number of studies using VBM to investigate associations between brain structure and decision making in healthy individuals. Additionally, studies utilising VBM, have been conducted using medium (Sun et al., 2018 - *N* = 350) to low sample sizes (Koehler et al., 2015 – *N* = 41). Given the surrounding literature highlighting the potential issues with using small samples sizes within neuroscience (Button et al., 2013; Lorca-Puls et al., 2018), such as; low statistical power, increased effect sizes, low reproducibility and inflated false discovery rate (see Button et al. 2013), there is sufficient scope to assess the morphometric correlates of decision making on a large sample size.

One of the main limitations surrounding several of the neuroscientific studies mentioned in this thesis is low statistical power. Given that publishing within any scientific field is a competitive enterprise, and that studies are more likely to be published with a significant result ($p = <.05$), this has led to scientists publishing studies that are often underpowered (Button et al., 2013). As a result, this leads to false positives and low reproducibility rates due to the quick execution of the studies and low sample sizes as a resulting factor. One assessment of this issue revealed that a typical underpowered dataset would reveal a false positive result at a rate equivalent to 97% (Sullivan, 2007). In order to address this issue within neuroscience literature, the current study will reproduce

the results of the previous study by Sun et al. (2018) using a large well-characterised sample of 851 participants gathered from the Human connectome project (HCP). Owens et al. (2017) utilised HCP data, and a large sample size to replicate prior studies investigating the relationship between grey matter volume and delay reward discounting, identifying several disparages in comparison to the results of previous literature conducted on small samples. The authors conclude that one reason for the difference in results is due to the underpowering of studies within neuroscience. Yet, due to the limited number of studies using high sample sizes, this conclusion is only speculative. Therefore, there exists a need for more research with high-powered studies to elucidate whether these disparages within the literature are due to underpowered studies or other factors. Given the current study aims to replicate a prior investigation using a high sample size, the current study aims to contribute findings to the process of addressing this issue within the field of neuroscience.

In the current study we aimed to investigate the neuroanatomical correlates of the effect previous outcomes to rewards or losses had future decision making in a large cohort of healthy individuals. Similar to Owens et al. (2017), we utilised the Human Connectome Project (Van Essen et al., HCP, 2013) data. The Human connectome project is a large open-access dataset, developed by Van Essen et al. (2013) in order to make neuroimaging data available to researchers to further understand the underlying neural correlates of cognition, behaviour and other specialties. To investigate how grey matter volumes relate to switching behaviour following either a win trial or a loss trial, the current study downloaded and utilised structural scans and behavioural data from the HCP dataset. In order to measure switching behaviour, we used an adapted version of Delgado et al. (2000) reward paradigm previously used in numerous fMRI studies (May et al., 2004; Delgado, Locke, Stenger & Fiez, 2003; Forbes et al., 2009). The paradigm consists of a gambling task whereby participants were instructed to guess whether the value of a card is either higher or lower than 5. Within this task we aimed to replicate the results found by (Sun et al., 2018) by measuring the frequency in which participants switch following wins versus losses. To build on previous research (Sun et al.,2018; Adrián-Ventura, Costumero, Parcet & Ávila, 2019) the current study measured the frequency participants switch when the previous trial was a reward in comparison to the frequency of switches following a punishment trial. The current study will provide a novel approach to understanding how prior outcomes effect future decision making, regardless of overall task performance.

Hypotheses

1. As in Sun et al. (2018), there will be a significant positive correlation between grey matter volume of the Frontal Pole, Posterior Cingulate, and Left Insula and the tendency to switch behaviour in the gambling task (regardless of preceding trial).

2. As in Sun et al. (2018), there will be a significant negative correlation between grey matter volumes of the Medial Temporal Lobe and Right Insula Cortex in relation to switching frequency (regardless of preceding trial).

3. There will be a significant correlation between grey matter volumes within the Right Insula Cortex and Medial Temporal Lobe and increased frequency of switching after loss trials (punishment).

Methodology and research design

4.1: Participants or Subjects

Participants were taken from Human Connectome Project (HCP) 1200 subject release data set (Van Essen et al. HCP, 2013). The HCP data set is an existing, open source, secondary dataset that includes T1 structural MRI scans, demographic and behavioural data for 1200 participants (aged 22-35). Our study utilised T1 scans and behavioural data for 851 participants (461 Females and 390 males) see data exclusion section for further exclusion criteria). Participants were medically assessed and had no significant history of psychiatric disorder, neurological disorders, cardiovascular disease, or Mendelian genetic disease (e.g., cystic fibrosis, xeroderma pigmentosa and stickle cell anaemia). Record of assessment is given within the HCP manual and release publications (Van Essen et al. HCP, 2013). Due to the current study utilising secondary data from the HCP project, the current study did not control any of the scanning criteria set out by the HCP dataset. The current study was conducted with approval from the University of Huddersfield's ethical review procedure in compliance with APA and BPS ethical standards. The current study was also preregistered on the Open Science Framework (https://osf.io/ - see appendix A)

4.2: Reward Paradigm

The behavioural measures consisted of an adapted version of Delgado et al. (2000) reward paradigm that was used as part of the Human Connectome Project, and data publicly available, which the current study utilised. The task is a reward paradigm, that originally assessed how people responded to rewards and losses whilst undergoing an fMRI scan. The way in which we analysed the data was adapted in a novel fashion to suit the nature of the current study (see below).

In this behavioural task participants were instructed to predict whether a hidden number behind a playing card was greater or less than the value of 5. Trials began with a question mark (presented for up to 1500 ms) indicating the participant had to make a guess. In order to make a prediction that the card was higher they were instructed to push the button in their right hand, and to make a prediction the card was lower, they were instructed to push the button in their left hand. Feedback numbers ranged from 1 to 9 to equate a 50% balance either side of the value of 5. For every

successful prediction the participant gained $1, and lost $0.50 for every unsuccessful prediction. There were three types of trials, reward trials to which the participant were rewarded $1, loss trials where they lost $0.50, and neutral trials where the number 5 would appear and participants did not gain or lose any reward. The feedback of each trial was predetermined by the computer categorising trials into either a reward trial, punishment trial or neutral event. The feedback was presented for 1000 ms, followed by an intertrial interval in which a fixation ("+") was presented for 1000 ms (See Figure 1). The task feedback is equal in probability (50% reward trials, 50% loss trials) therefore unlike previous studies there is no optimal strategy to maximise rewards and mitigate losses.

The task was presented in blocks of 8 trials that were either mostly reward or mostly loss, but still contained a mix of trial types. In each of the two runs there were two mostly reward and two mostly loss blocks interleaved with four fixation blocks (duration 15 sec). Each participant completed a total of 64 trials. The task data was collected as part of the HCP dataset and the data made available for researchers to download from the HCP site. (see release documentation for further information – HCP Manual).

Figure 1. Gambling task used in HCP data set. Feedback based on a trial in which a participant picked 'higher' on both reward and punishment trial

In order to assess switching behaviour, the total number of switches after both reward and punishment trials were computed in MATLAB for each participant from the raw behavioural data. Responses preceding and after neutral trials were excluded from the analysis as responses after these trials do not assess switching behaviour to either a reward or a punishment. Therefore, for each participant 6 trials (neutral trials) were discounted leaving a total of 58 trials (29 reward and 29 punishment) for each participant that were included. These Figures were then converted into percentages and imputed into the regression model.

4.3: Structural MRI data collection procedure

Structural MRI scans were acquired using a customised Siemens 3.0 T "Connectome Skyra" (Siemens AG, Erlanger, Germany) using a 32-channel head coil located at Washington University in St Louis. Two separate averages of the T1-weighted image were acquired using 3D, gradient echo pulse sequence (MPRAGE) with a resolution of 0.7 mm3 isotropic (FOV = 224 × 224, matrix = 320 × 320, 256 sagittal slices; TR = 2400 ms and TE = 2.14 ms). The use of T1 structural MRI scans are suitable for the current analysis as it allows us to segment the data into separate tissue volumes; grey matter, white matter and cerebrospinal fluid (see diagram below)

Following the structural MRI, all scan images were reviewed by a HCP technician to ensure scans did not have any problems (i.e. excessive data noise from substantial movement and artefacts). If any problems were identified the original scan was discarded and a new structural scan was initiated immediately. After any immediate issues were identified with scan acquisition, all scans were examined by HCP quality control experts. They assessed the scans based on motion, other previously unidentified artefacts, image quality and accuracy of defacing. From this assessment scans were given a score from 1 to 4 (1; poor 2; inadequate, 3; good, and 4; excellent). Scans were all rated above the value of 3 indicating they had good quality control, ensuring a good signal to noise ratio. For further information on quality control procedure see HCP quality control documentation; Marcus et al. (2013).

The structural MRI data collection procedure outlined above was taken from the HCP Data set structural pre-processing information, see manual (Van Essen et al. HCP, 2013). The current study utilised this data however was not involved with the acquisition of these scans, nor the parameters set within this procedure.

4.4: VBM pre-processing

Voxel based morphometry (VBM) was used in order to analyse grey matter volumes. The raw T1 data were re-processed using statistical parametric mapping software (SPM12; Wellcome Department of Cognitive Neurology, London, UK, https://www.fil.ion.ucl.ac.uk/spm/) implemented in MATLAB (Mathworks Inc., Natick, MA). Initially, T1 weighted images were segmented into grey matter, white matter and cerebrospinal fluid using an extension of the standard unified segmentation model in SPM12. The resulting grey matter volumes from the segmentation step were normalised to Montreal Neurological Institute (MNI) standard space generating template images and flow fields. Grey matter volumes were spatially normalised across all participants using the DARTEL algorithm (Diffeomorphic Anatomical Registration Through Exponentiated Lie Algebra; Ashburner, 2007) voxel size: 1.5 mm × 1.5 mm × 1.5 mm in MNI space. Finally, the data was smoothed with an 8mm FWHM (full width half maximum) Gaussian Filter. Images were then modulated to create Jacobian scaled grey matter images using deformations estimated in the DARTEL step (see Figure 2 below).

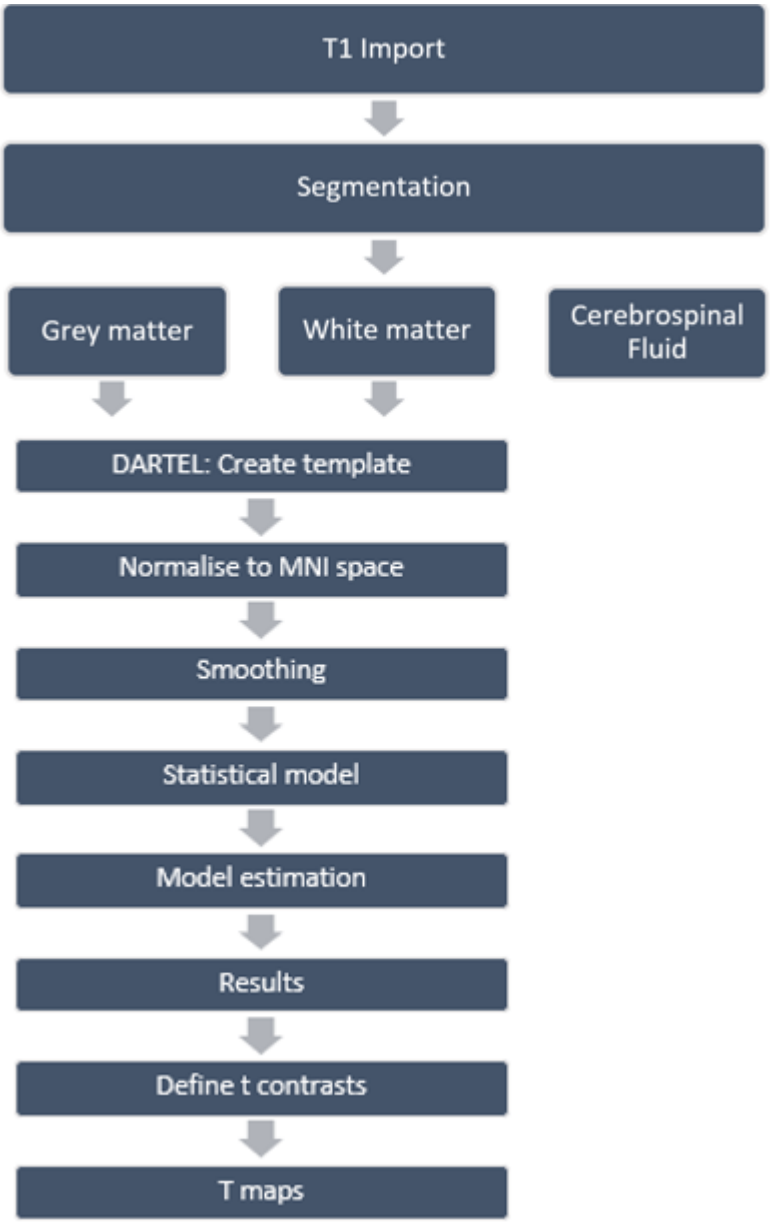


Figure 2. Diagram illustrating VBM pre-processing steps

4.5: Explanation of VBM pre-processing

4.6: Statistical analysis

In order to initially test the prevalence of switching behaviour within the sample, a paired samples t test was conducted to test the difference between switches after reward trials in comparison to switches after loss trials. Data normality was assumed (see Figure 1 and 2). Statistical analysis was conducted using IBM SPSS 26 (IBM, SPSS Statistics, Chicago, IL, USA).

Whole brain corrected statistical analysis was performed on normalised and smoothed grey matter maps using SPM12. A multiple regression model was set up in SPM12 in order to assess the association between whole brain grey matter volumes against the percentage of switches following reward trials versus loss trials, controlling potential confounding variables of Total Intracranial Volume, age and gender. All variables were imputed into the regression simultaneously. Total intracranial volume was calculated by summing the values of grey matter, white matter, and cerebrospinal fluid using the 'tissue volumes' option within SPM12. Total intracranial volume was added as a covariate within the global calculation option in SPM12. Absolute masking was used at a threshold of 0.2 and no explicit mask was added.

4.7: Data exclusion

A total of 889 participants were identified as having both T1 scans and behavioural data on the gambling task within the HCP dataset. Following further investigation we found 16 participants had incomplete behavioural data and 3 were missing a full T1 structural scan. Within the data set 19 participants measured as a 100% response rate on either option (higher or lower). Any participants that had 100% response rate on one of the options were discounted as responses do not result in data suitable for the purposes of the experiment. After all data exclusions, sample size for this study was 851.

4.8: Ethical procedure

This study was approved by the University of Huddersfield's ethical review procedure. The data used secondary data taken from the HCP data set. In line with the guidelines set out by HCP ethics (Van Essen, 2013) all T1 scans and behavioural data was kept secure within a password protected folder. HCP assigns a unique reference number in order to protect participant's anonymity. All data was discarded after data analysis was conducted and participants remained anonymous conforming to GDPR regulations.

4.9. Data consolidation and reconciliation

The current study required a total of 1702 (851 T1 files and 851 behavioural files) files to be downloaded and converted into a usable format for data analysis. In order to mitigate any data loss and keep track of data files, scripts were written using both Virtual Basic (VBA) and MATLAB. For the first analysis, behavioural results had to be converted from text file into Excel files. Due to the large

amount of datafiles containing behavioural data, they required a script to be written to convert them into workable formats. In order to do this, VBA code was written to convert 1702 files (each subject had two runs of data; run1 and run2) and were then transferred to the server at the University of Huddersfield in order to ensure data security. Following the conversion of these files, code was executed in MATLAB to extract information of interest. This included (run number, Trial type, consecutive smaller guesses, consecutive larger guesses and HCPID). This was then converted to a text file and loaded into the regression model within SPM12. In order organise T1 structural scans, 851 files were renamed, using basic code in VBA, adding the HCPID to each file, along with a "+" symbol in order to symbolise files that will be used within the analysis to avoid data loss. In order to ensure accurate detection and transfer of the required files, data reconciliation was also conducted in comparison with the HCP data manifest before data input into analysis software to ensure no loss of data (See Appendix B for script examples).

Results

5.1: Behavioural Results

Initially, in order to assess the prevalence of switching behaviour within the HCP reward paradigm, percentage frequency of switches both overall and following rewards and punishments were computed from the behavioural data. The results showed that overall, participants displayed a switching frequency of 39.54% and a stick frequency of 60.46%. Moreover, switching behaviour was marginally lower following a punishment trial in comparison to a reward trial. A paired samples t-test revealed there was a significant difference between amount of switches after rewards (M = 50.29% SD = 4.90) compared with amount of switches after punishments (M = 49.78%, SD =4.17), $t(850)= 3.121$, $p = .002$ (two-tailed). The mean difference between the two conditions was 0.597 with a 95% CI ranging from 0.222 to 0.972. The eta statistic (.01) indicated a small effect size (see Table 1 & Appendix D).

Table 2. *Descriptive statistics showing switch frequencies of reward and punishments separated by sex and age range*

Demographics	**Mean Switch after reward (Standard deviation)**	**Mean switch after punishment (Standard deviation)**
Sex		
Male (n= 390)	11.48 (4.962)	10.54 (4.327)
Female (n = 461)	12.00 (4.829)	11.70 (3.954)
Age		
22-25 (n = 187)	11.35 (5.152)	10.40 (4.493)
26-30 (n = 336)	11.57 (4.943)	11.07 (4.160)
31-35 (n = 290)	12.26 (4.643)	11.76 (3.909)
36+ (n = 8)	11.76 (4.895)	11.17 (4.167)

5.2: VBM Results

A whole brain corrected VBM analysis (FWE = .05) was conducted to assess whether grey matter volumes were associated with switching frequencies after both reward and punishment trials. The VBM analysis revealed greater switches after punishment negatively correlated with grey matter volume (Table 3). VBM t maps were also created for both positive and negative grey matter clusters associated with switches following rewards, however no clusters were identified within this analysis. Moreover, no positive grey matter volume clusters were identified to be associated with switches following punishments. Within the regression both age and gender were included as covariates of interest, however no associations were identified between grey matter volumes or switching in relation to age or gender.

Table 3. Brain regions with negative cluster volumes associated with punishment switch

Brain region	**Hemi**	**Z score**	**Cluster size**	**X**	**y**	**z**	***p***
Superior Temporal Gyrus (BA22)	L	5.04	272	-44	-21	2	0.002
Occipital Lobe, Lingual Gyrus (BA18)	L	5.06	99	-32	-72	-12	0.009
Superior Occipital Gyrus (BA19)	L	4.94	36	-33	-80	-26	0.021
Insula (BA13)	R	4.57	35	39	-23	6	0.021
Middle Temporal Gyrus (BA21)	R	4.46	6	56	-53	-5	0.039
Parahippocampal Gyrus (BA36)	L	4.41	5	36	-32	-20	0.04

Cluster threshold = .05 , intensity = 4.48 and cluster size threshold = 5; FWE = .05

The results presented in Table 3 show reduced grey matter volumes within the Left Superior Temporal Gyrus (r = - 0.1741, *z = 5.04, p= <.05),* Left Lingual Gyrus; Medial Occipital Lobe (r = - 0.1741, *z = 5.06, p = <.05*), Left Superior Occipital Gyrus (r = - 0.1725, *z = 4.94, p = <.05*), Right Insula (r = - 0.1626, *z = 4.57, p= <.05*), Right Middle Temporal Gyrus (r = - 0.1563, *z = 4.46, p = <.05*) and Left Parahippocampal Gyrus (r = - 0.1556, *z = 4.41, p = <.05)* correlated with increased frequency of switches after punishment trials after correction for family wise error (FWE = .05). See Figures (3,4,5,6,7, and 8) showing statistical maps of grey matter volumes that correlated with frequency of switching after punishment. Slices were chosen in order to clearly identify brain regions associated with switches after punishment trials. All statistical maps (images) were shown in radiological format (reflective inversion, I.e: Left = Right, Right = Left).

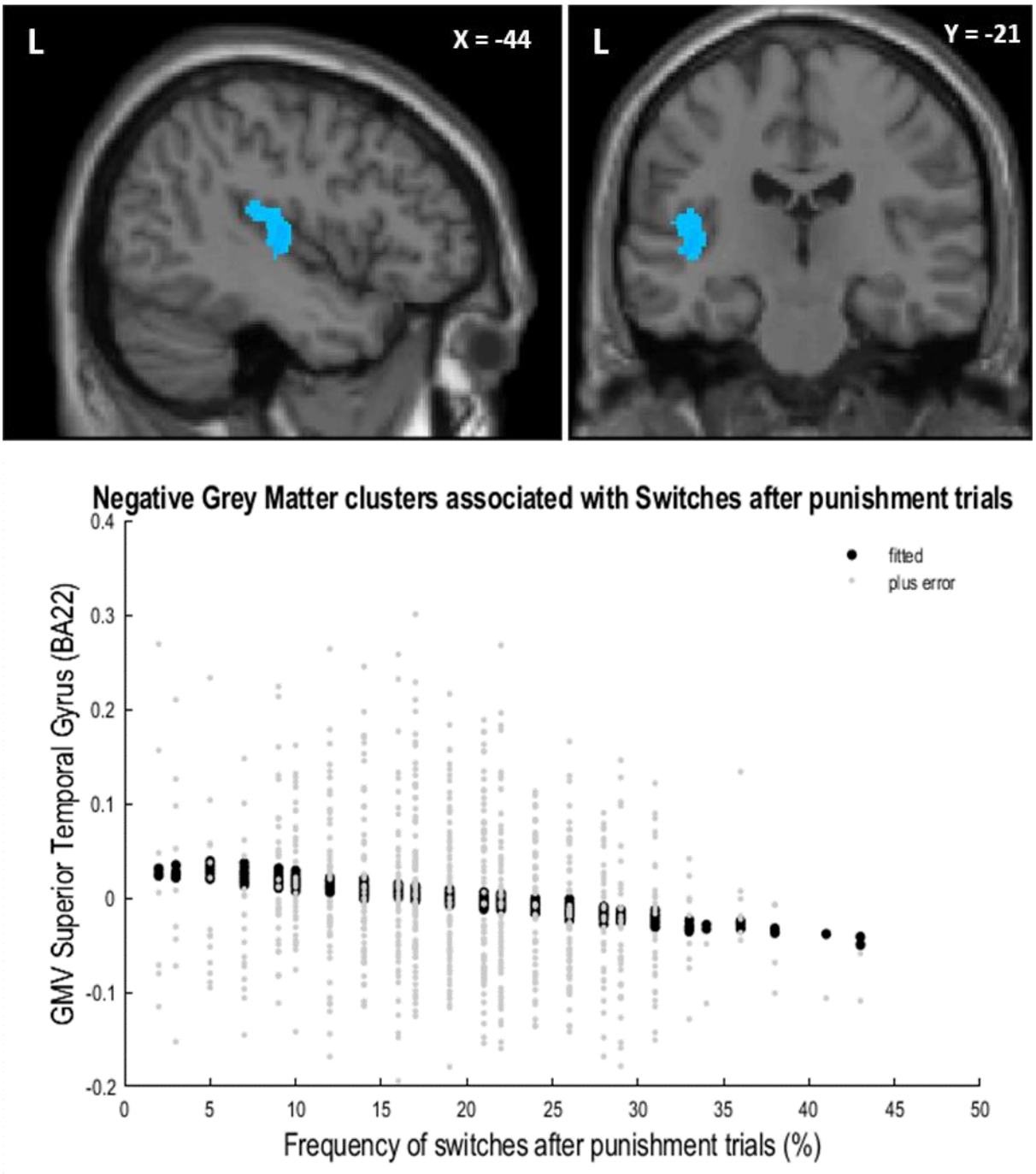


Figure 3. Above: Whole brain statistical maps showing negative correlations between GMV and switching after punishment (Sagittal X, Coronal Y). Slices chosen to best display area of interest. Below: Plot comparing grey matter cluster volumes in Left Superior Temporal Gyrus ($r = -0.1741$) against switches after punishment (FWE = .05):

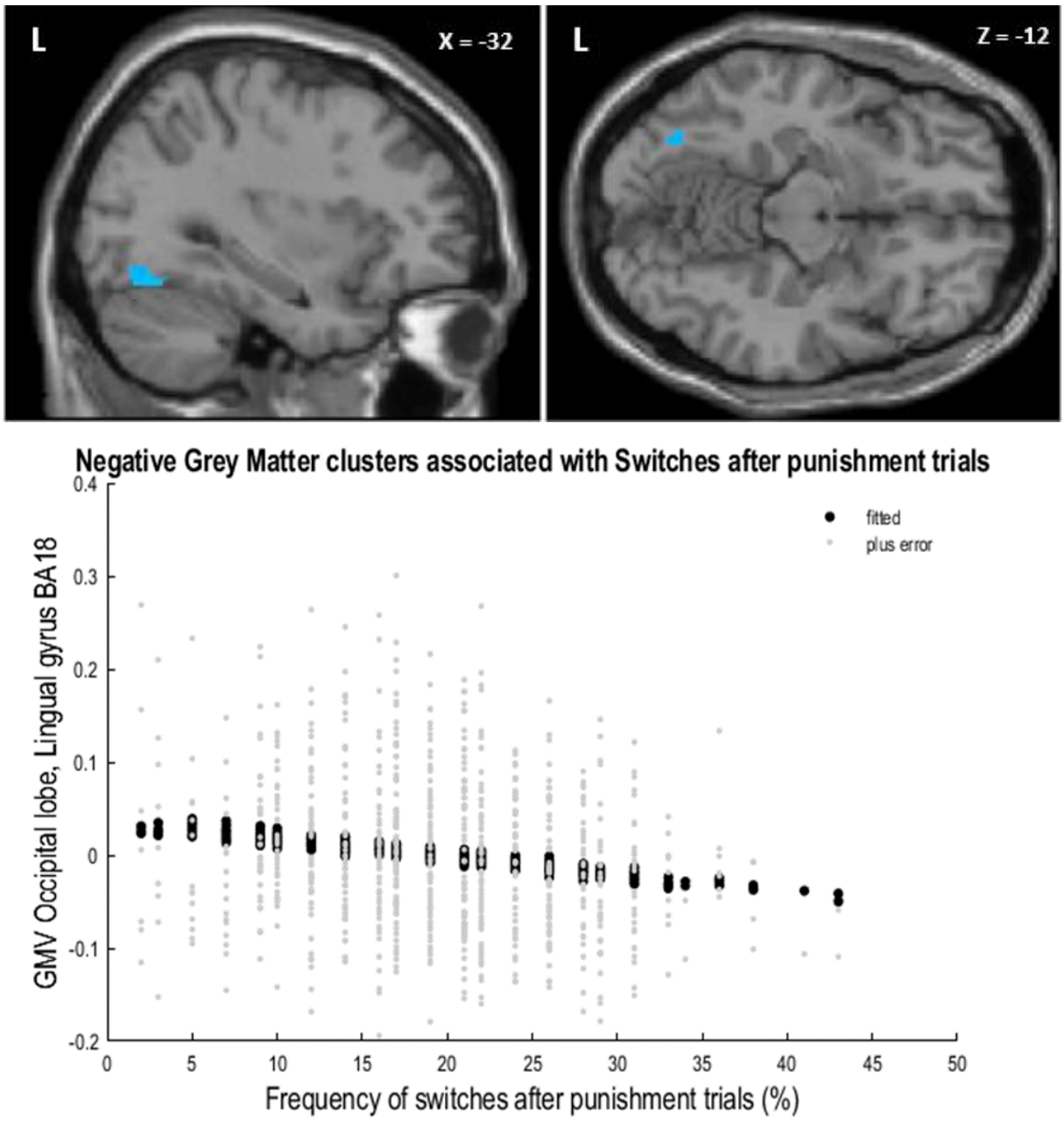


Figure 4. Above: Whole brain statistical maps showing negative correlations between GMV and switching after punishment (Sagittal X, Transverse Z). Slices chosen to best display area of interest. Below: Plot comparing grey matter cluster volumes in Left Lingual Gyrus(r = - 0.1741) against switches after punishment (FWE = .05)

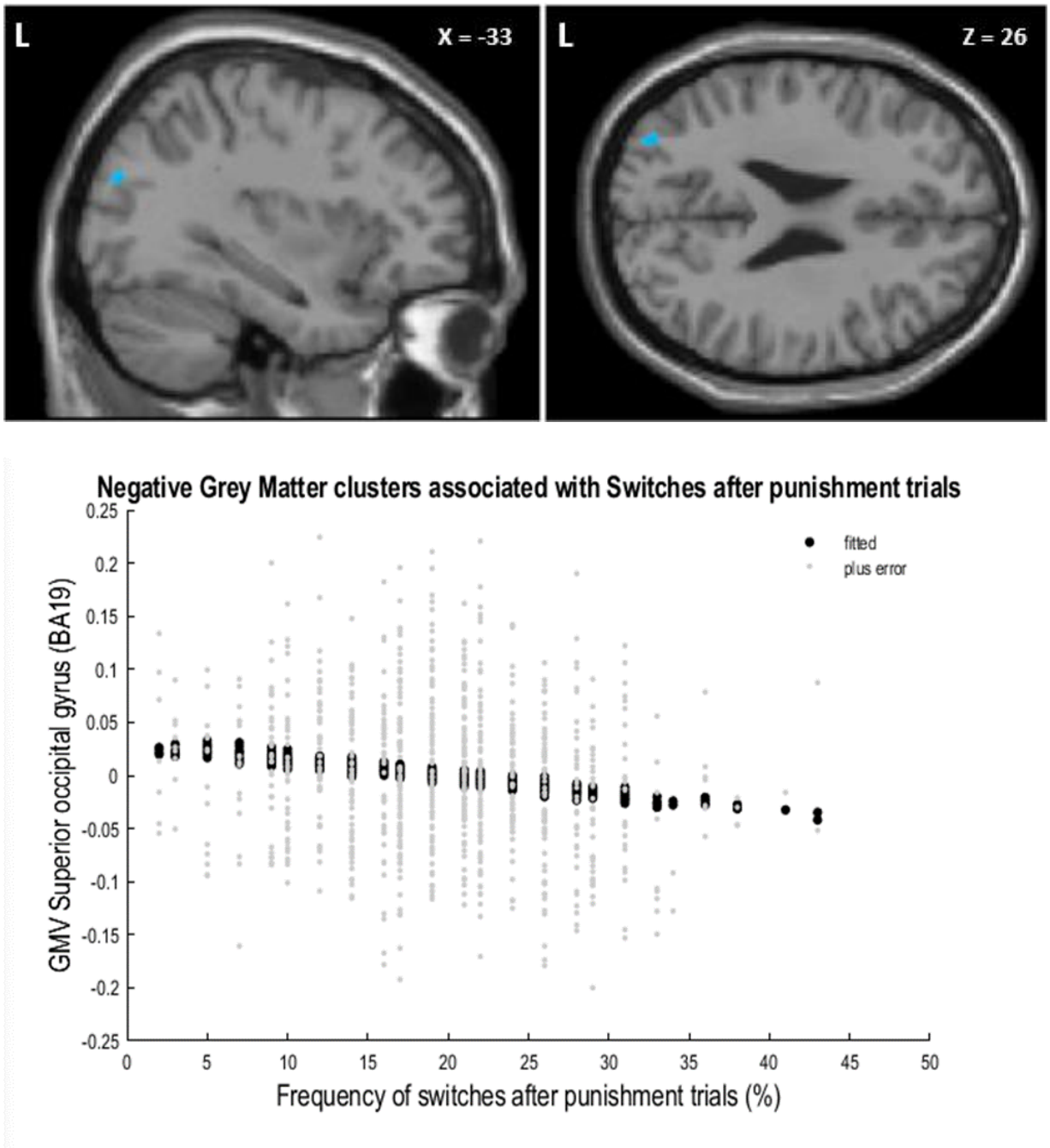


Figure 5. Above: Whole brain statistical maps showing negative correlations between GMV and switching after punishment (Sagittal X, Transverse Z). Slices chosen to best display area of interest. Below: Plot comparing grey matter cluster volumes in Left Superior Occipital Gyrus ($r = -0.1725$) against switches after punishment (FWE = .05)

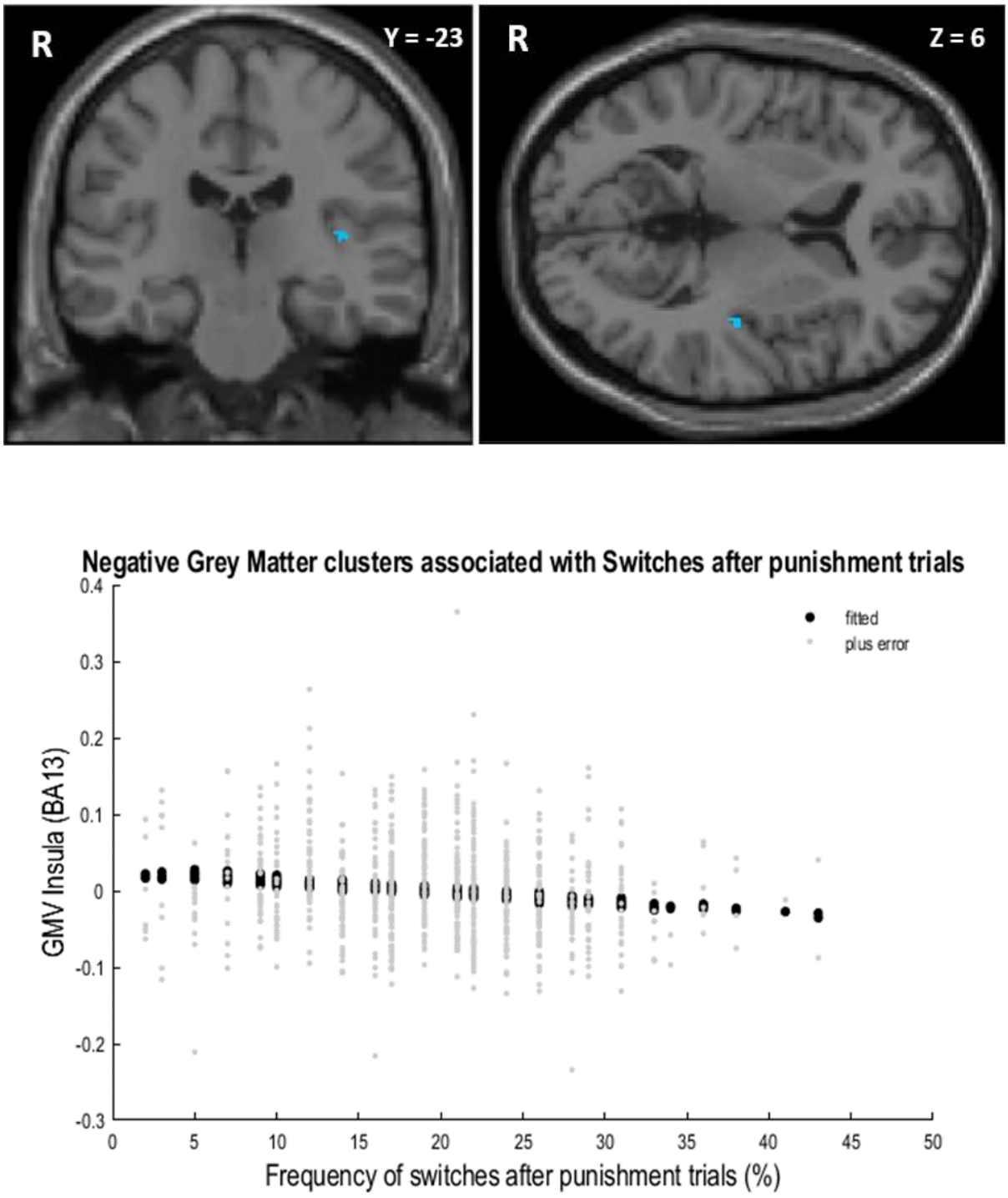
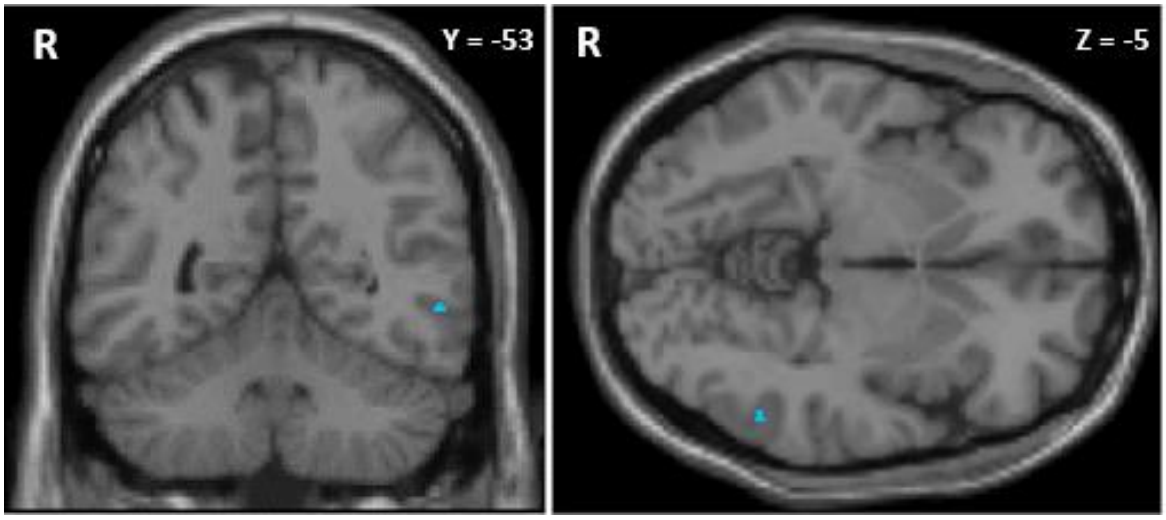


Figure 6. Above: Whole brain statistical maps showing negative correlations between GMV and switching after punishment (Coronal Y, Transverse Z). Slices chosen to best display area of interest. Below: Plot comparing grey matter cluster volumes in Right Insula (r = - 0.1626) against switches after punishment (FWE = .05)



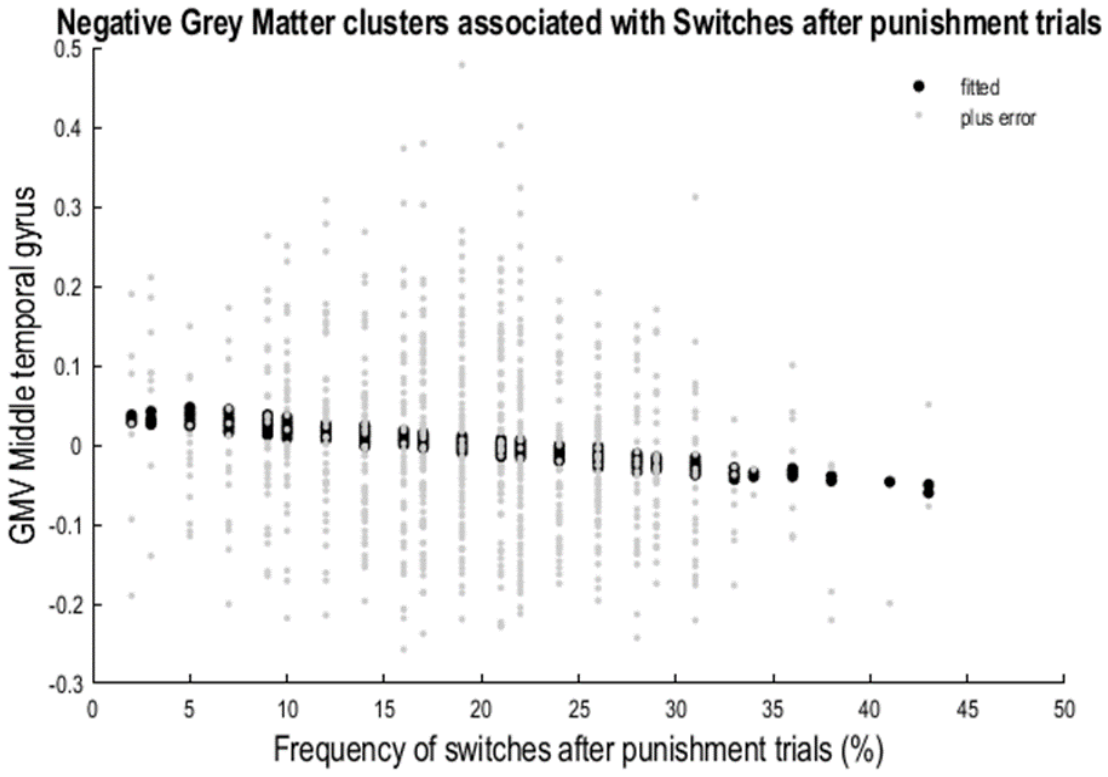
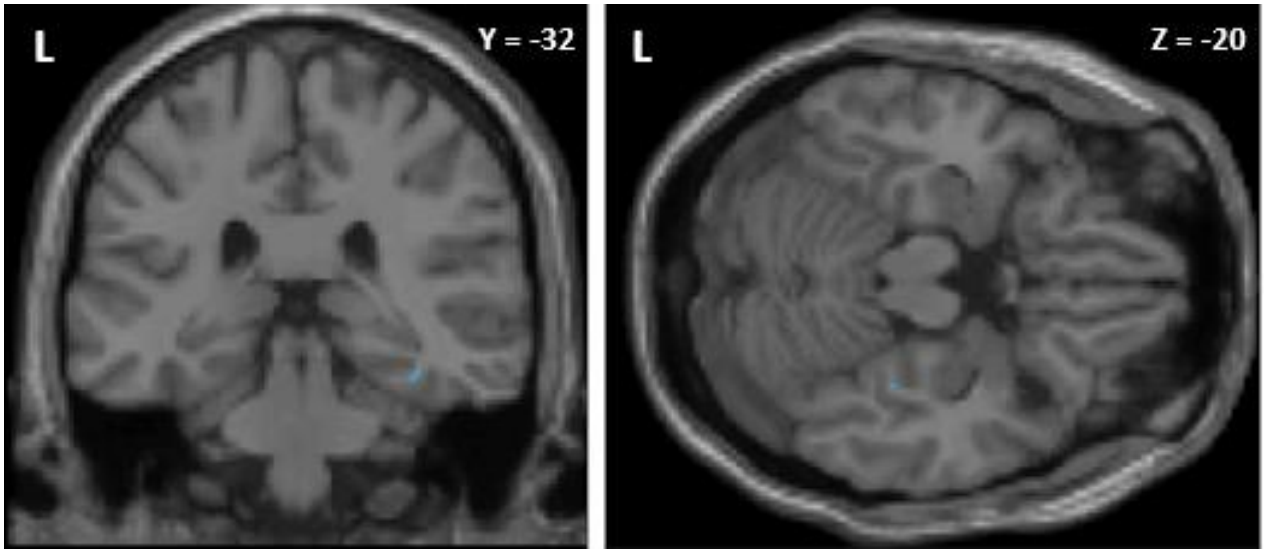


Figure 7. Above: Whole brain statistical maps showing negative correlations between GMV and switching after punishment (Coronal Y, Transverse Z), Slices chosen to best display area of interest. Below: Plot comparing grey matter cluster volumes in Middle Temporal Gyrus (r = - 0.1563) against switches after punishment (FWE = .05)



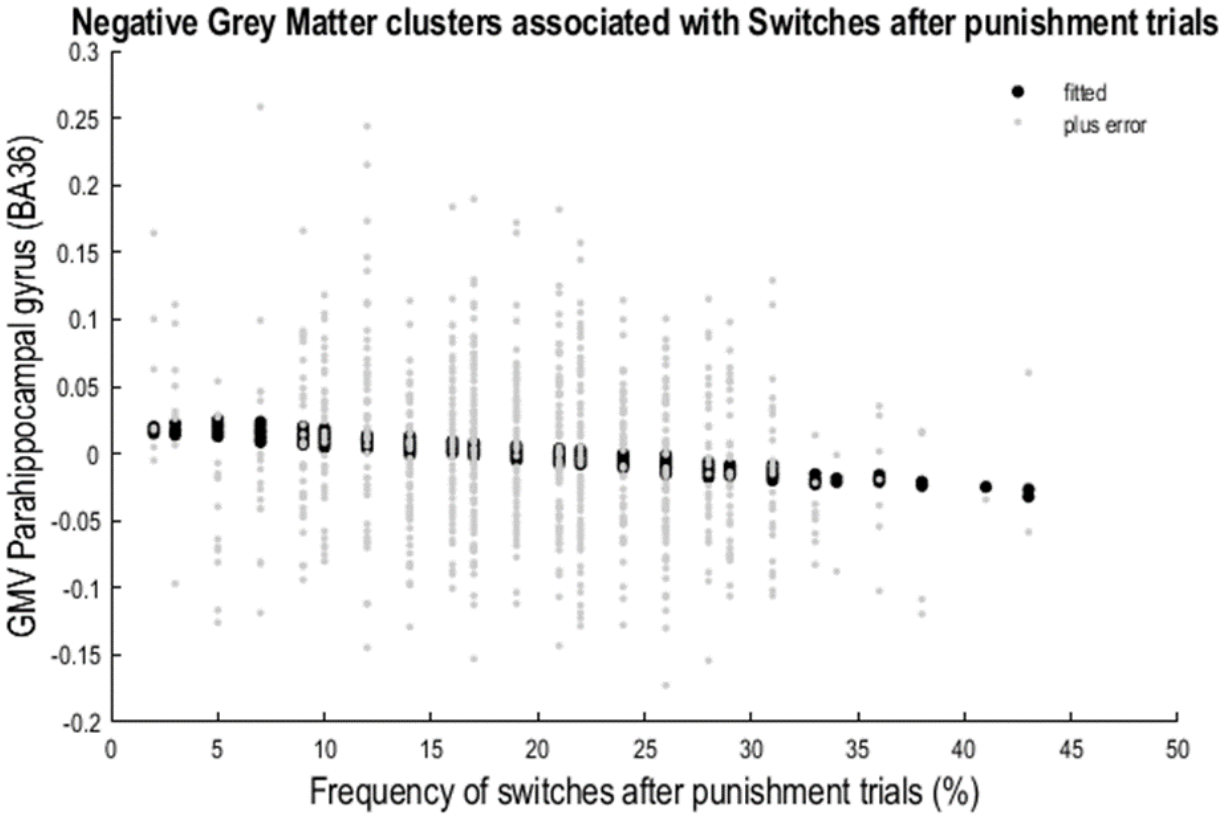


Figure 8. Above: Whole brain statistical maps showing negative correlations between GMV and switching after punishment (Coronal Y, Transverse Z). Slices chosen to best display area of interest. Below: Plot comparing grey matter cluster volumes in Left Parahippocampal Gyrus (r = - 0.1556) against switches after punishment (FWE = .05)

5.3. Neurosynth

Finally, in order to better understand the association between the significant areas identified within the previous VBM analysis, task co-activation meta-analyses were conducted within Neurosynth (https://www.neurosynth.org/locations). Neurosynth is a large-scale brain mapping database containing fMRI data, extracted from previously published articles, that allows for comprehensive meta-analyses based analysis on a region of interest. The resulting data reveals other brain regions. within previous literature utilising fMRI, that have showed common activations associated with the region of interest.

The purpose of utilising Neurosynth within the current study, was to investigate whether the areas identified within our VBM analysis were involved in any networks previously identified within fMRI literature. Following the input of MNI coordinates for each region of interest identified within the VBM, Neurosynth analysis identified correlations within the Insula and Lingual Gyrus for five of the six areas identified within the VBM analysis (see Figures; 9, 10, 11, 12, 13 and 14). The Superior Occipital Gyrus was the only area not to show activation within these regions (see Figure 11). Neurosynth analysis also revealed other coactivations with areas previously shown to be involved in reward processing such as; Middle Frontal Gyrus (Koehler et al., 2015), Frontal regions (Bechara, Damasio, Damasio & Anderson, 1994) and Anterior Cingulate Cortex (Campbell-Meiklejohn, Woolrich, Passingham & Rogers, 2008).

Neurosynth co-activation meta-analyses of all regions identified within the VBM analysis were set at a false discovery rate of p <0.05. At the time of analysis Neurosynth had 150,000 brain regions, in 14371 studies, consisting of 507891 activations (analysis conducted on 14th June 2020). The blue areas (white identifies seed region) within the Figures display positive co-activations, no negative co-activations were found in the analyses completed. See Figures Below (9, 10, 11, 12, 13 and 14).

Given the Insula showed meta-analytic coactivations within the majority of the brain regions identified within the current VBM, we conducted a further analysis using MRIcroGL (Rorden, 2012). Within MRIcroGL, Neurosynth maps were combined and overlayed to form one image in order to accurately determine which regions showed common meta-analytic coactivation within all 6 Neurosynth coactivation maps. The MRIcroGL map revealed the Insula as the most commonly activated region throughout the coactivation maps (see Figure 15).

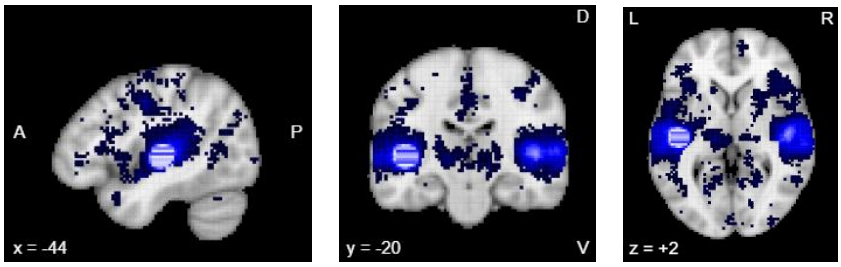


Figure 9. Neurosynth co-activation meta-analysis of the Left Superior Temporal Gyrus (BA22; MNI coordinates: -44, -21, 2) thresholded at false discovery rate criterion of $p < 0.05$. Figures display activation within the Bilateral Insula, Left Lingual Gyrus, Bilateral Middle Temporal Gyrus, Right Anterior Cingulate and Right Middle Frontal Gyrus (Colour key: white; represents seed region, blue; represent the regions with meta analytic coactivation).

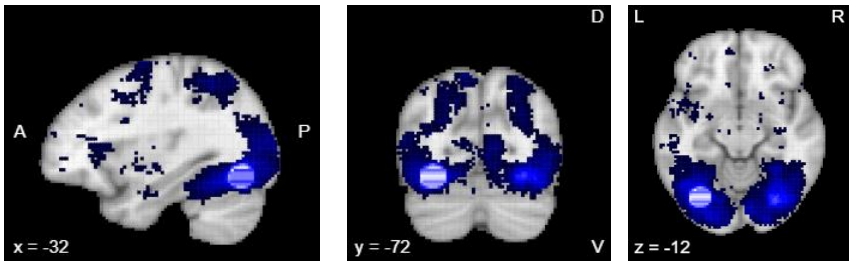


Figure 10 . Neurosynth co-activation meta-analysis of the Left Occipital Lobe, Lingual Gyrus (BA18; MNI coordinates: -32, -72, -12) thresholded at false discovery rate criterion of $p < 0.05$. Figures display activation within the Motor Cortex, Cingulate Cortex, Parietal Lobe, Bilateral Medial Temporal Lobe, Bilateral Superior Temporal Lobe, Middle Occipital Gyrus, Left Parahippocampal Gyrus, Putamen, Bilateral Insula Cortices and Medial Frontal Gyrus (Colour key: white; represents seed region, blue; represent the regions with meta analytic coactivation).

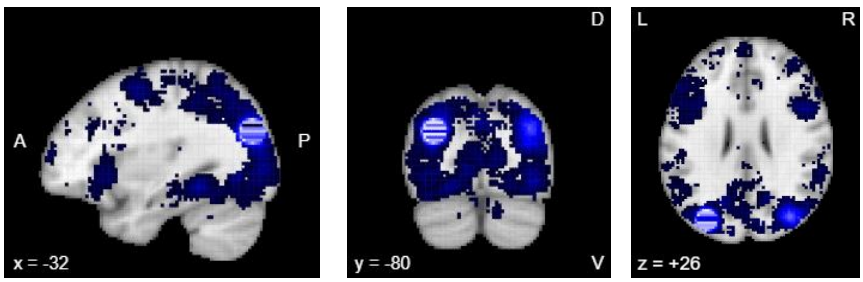


Figure 11. Neurosynth co-activation meta-analysis of the Left Superior Occipital Gyrus (BA19; MNI coordinates: -33, -80, -26) thresholded at false discovery rate criterion of $p < 0.05$. Figures display activation within the Bilateral Frontal Lobe, Brainstem, Cingulate Gyrus and Right Occipital Lobe (Colour key: white; represents seed region, blue; represent the regions with meta analytic coactivation).

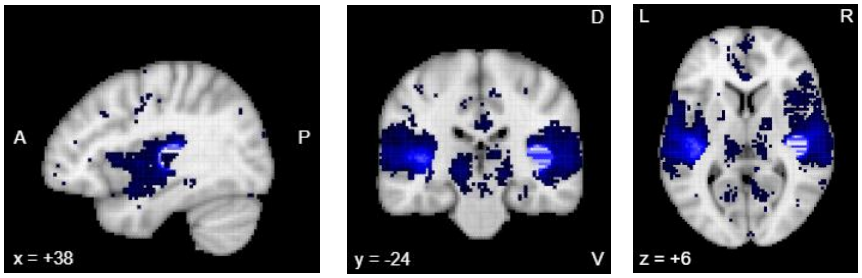


Figure 12 Neurosynth co-activation meta-analysis of the Right Insula (BA13; MNI coordinates: 39, -23, 6) thresholded at false discovery rate criterion of $p < 0.05$. Figures display activation within the Left Insula, Lingual Gyrus, Bilateral Brain Stem, Bilateral Middle Frontal Gyrus (Colour key: white; represents seed region, blue; represent the regions with meta analytic coactivation).

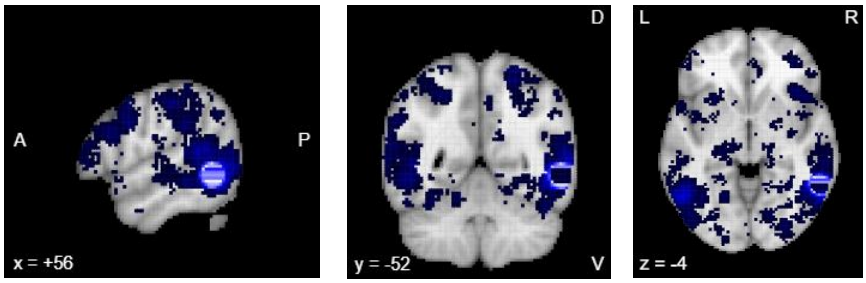


Figure 13 Neurosynth co-activation meta-analysis of the Right Middle Temporal Gyrus (BA21; MNI coordinates: 56, -53, -5) thresholded at false discovery rate criterion of $p < 0.05$. Figures display activation within the Bilateral Insula, Bilateral Middle Frontal Lobe, Right Brainstem, Bilateral Occipital Lobe, Bilateral Lingual Gyrus (Colour key: white; represents seed region, blue; represent the regions with meta analytic coactivation).

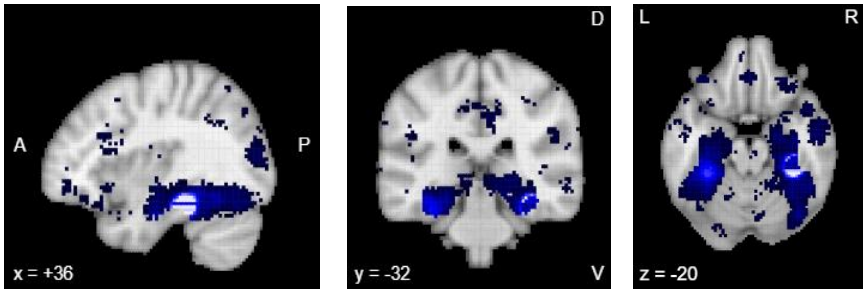


Figure 14. Neurosynth co-activation meta-analysis of the Left Parahippocampal Gyrus (BA36; MNI coordinates: 36, -32, -20) thresholded at false discovery rate criterion of $p < 0.05$. Figures display activation within the Left Parietal Lobe, Bilateral Occipital Lobe, Bilateral Middle Temporal Lobe, Left Inferior Frontal Lobe, Right Insula, Right Brainstem (Colour key: white; represents seed region, blue; represent the regions with meta analytic coactivation).

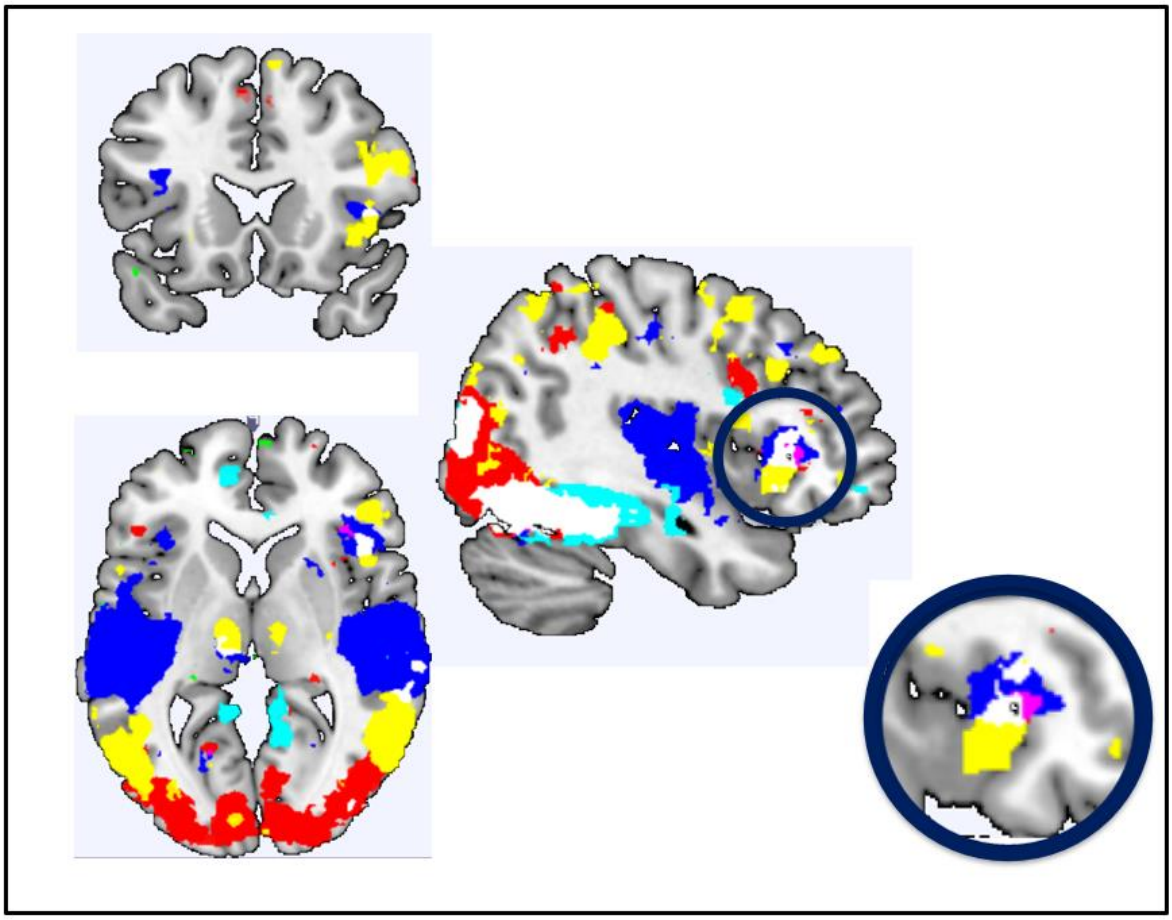


Figure 15. Overlap constructed within MRIcroGL (Rorden, 2012). Colours represent brain areas identified within all 6 Neurosynth meta analytic coactivation maps and reflect each coactivation matrix. Lower right corner; shows anterior Insula is a common area of activation indicated by the colour white.

Discussion

Using a novel approach, the purpose of this study was to identify the anatomical correlates of switching behaviour following previous reward and loss trials. Behavioural analyses revealed a higher stick frequency in comparison to switch frequency, when measuring general switching behaviour irrespective of the previous trial. Following a reward, the frequency of switches increased compared to those trials following punishments. In order to identify neuroanatomical correlates of switching, whole brain VBM analyses were conducted. When investigating the relationship between grey matter volumes and switching, irrespective of previous trials, no significant positive correlations were identified. Moreover, no significant negative correlations were identified regardless of previous trial, consequently rejecting the first and second research hypothesis. Interestingly, when investigating the relationship between whole brain grey matter volumes, and switching following rewards and punishments, as hypothesised, significantly lower grey matter volumes were seen within the right Insular and right Medial Temporal Lobe as well as reduced grey matter correlates within the Left Superior Temporal Gyrus, Left Lingual Gyrus and Left Superior Occipital Gyrus. Follow up analysis exploring fMRI co-activation analysis between regions that were strongly associated with switching were conducted within Neurosynth. We found these areas showed strong meta analytic coactivation with each other, findings which may indicate that these regions are integral in this type of decision making.

The behavioural results of the current study show a 60.46% stick rate and only a 39.54% switch rate irrespective of previous outcome, similar to the result Sun et al. (2018) found (57% average stick rate, 43% average switch rate). Given the similarities identified within the behavioural results, it is surprising the results identified by the VBM analysis conducted in the current study revealed no significant correlations between grey matter volumes and switching frequency, irrespective of previous trials. Although no associations in grey matter volume were found relating to general switching behaviour within the current study, we also evaluated the impact rewards and losses had on subsequent switching behaviour. The behavioural results show a significant increase in number of switches after rewards in comparison to switches after punishments. Increased frequency of switches following rewards may be a strategy in order to maximise reward outcomes and avoid losses. The results from the behavioural analysis may provide support for Prospect Theory (Kahneman and Tversky, 1979) as Prospect Theory suggests individuals are much more sensitive to losses than they are to potential gains. Therefore, participants may posit that switching after rewards may be a worthwhile strategy, as the subsequent impact of a potential loss would be less damaging.

Whole brain VBM analysis revealed several significant negative correlations between increased tendency to switch following punishments in six clusters comprising of the Right Insula, Right Medial Temporal lobe, Left Superior Temporal Gyrus, Left Lingual Gyrus, Left Parahippocampal Gyrus and Left Superior Occipital Gyrus. Similar to the results of Sun et al., (2018) the correlations identified within this study are weak correlations however, prior investigations show evidence that these areas identified are associated with similar types of behaviour. Within the field of decision making, the Insula has often been associated in the detection of aversive stimuli (Clark et al., 2008; Craig, 2009; Caria et al., 2010) and loss processing (Palminteri et al., 2012). In the current study, grey matter volumes within the Insula showed a significant negative correlation with frequency of switches after punishment. Similar findings were also reported by Markett et al. (2016) who identified increased loss aversion was associated with lower grey matter volumes within the Insula. Additionally, another VBM study (Nasiriavanaki et al., 2015), investigating structural correlates of decision making, found a positive correlation with the grey matter volumes within the Anterior Insula and increased risk-taking behaviour and inversely, found negative grey matter volumes in the Anterior Insula correlated with less risk-taking behaviour. Although the current study did not measure loss aversion, the results identified by previous studies (Nasiriavanaki et al., 2015; Markett et al., 2016) may help elucidate our findings, as individuals with lower grey matter volumes within the Insula may show increased switches following a previous experience of a punishment, as it is an undesirable outcome and may be viewed as a more aversive consequence. Evidence for the involvement of the Insula, relating to the previous outcomes have been corroborated within lesion studies, suggesting disruption of Insula function is associated with decision making that is unaffected by previous experiences. Clark et al. (2014), found that healthy individuals displayed increased use of the gamblers fallacy strategy whereas lesion patients showed decision making strategies that were seemingly independent from prior outcomes. Furthermore, Clark et al. (2008) found lesions located in the Insula led to a disruption in the ability to update future decision making strategies based on the probabilities of occurring a loss in a gambling task. Other lesion studies have also shown comparative findings (Weller, Levin, Shiv, & Bechara, 2007) highlighting that Insula damage is associated with reduced sensitivity to prior outcomes. These studies provide some evidence relating to the involvement of the Insula in tracking the previous consequences of a decision, and ultimately could explain why increased switch frequency was associated with lower grey matter volumes within this area. However, any comparisons between lesion studies and the results found within the current study should be taken with a degree of caution, as no lesion is directly comparable to another (Rick, 2011). Correlates between punishment switches and reduced Insula volume may be a result of a unique effect resulting in individuals with lower grey matter volume to behave differently

in switching tasks. Although previous research provides good evidence for the implication of the Insula in loss processing, it is currently unclear as to the extent structural differences in grey matter volume within the Insula affect switching. Future studies are needed to further understand the involvement of this area in increased switching following punishment trials both in healthy and clinical populations in order to further solidify the relationship between grey matter volumes and switching behaviour.

An alternative explanation of the associations found within the Insula could be due to subjective versus objective value. Within the current task, participants could either win $1 or lose $0.50. Objective value of a reward/loss is the amount of reward given or amount of money lost, whereas the subjective value of a reward is how the participant personally views the reward/loss. This can be influenced by several factors such as; an initial reference point relating to how much money they currently have (Kahneman and Tversky, 1979), or inborn beliefs and attitudes (Nasiriavanaki et al., 2015; Dreher & Tremblay, 2017). Thus, individual differences in these values could have affected how loss averse someone is, which may result in increased switches following punishments. Evidence to support (Craig, 2009) suggests that the Right Insula Cortex is involved in risk prediction and visual and auditory awareness of the present moment. It is possible that individual differences relating to how an individual views receipt of either a reward or loss, may have had an impact on subsequent switching frequency, given the findings from previous studies (Kahneman and Tversky, 1979; Nasiriavanaki et al., 2015; Dreher & Tremblay, 2017). Furthermore, Harrison et al. (2016) found that inducing a negative mood within participants can increase Insula activity when they are presented with a punishment, suggesting that they see the punishment more negatively when in a negative mood in comparison to a positive mood. Self-esteem can also be a contributing factor, showing individuals with higher self-esteem, are more likely to keep going when presented with a threat or a loss whereas individuals with lower self-esteem are impacted by the threat of losses more, and are more likely to be risk averse (Josephs, Larrick, Steele & Nisbett, 1992). Future studies could investigate the impact of individual differences such as financial position, values and mood influences have on switching behaviour and how this relates to brain structure of regions such as the Insula.

The current VBM analysis also revealed lower grey matter volumes within the Parahippocampal Gyrus and increased switching after punishment trials. Similar to the Insula, there is also evidence to suggest the Parahippocampal region may be involved in emotional processing. A study by Lutz et al. (2014), investigating the neural correlates of emotion regulation to mindfulness-based practice found that, during perception of negative stimuli, reduced activation was seen within both the amygdala, Insula and right Parahippocampal Gyrus following mindfulness practice in comparison

with no intervention, providing evidence that these areas are associated with negative affect. This suggests that individuals who have less activation within both the Insula and Parahippocampal Gyrus are less affected by negative stimuli. This could explain why grey matter reductions were seen in relation to increased frequency of switching after punishments. Grey matter reductions within both the Insula and Parahippocampal Gyrus may result in differences in how an individual views a loss, leading to an increased tendency to switch following a punishment.

The Parahippocampal Gyrus may also be strongly connected to the ventromedial prefrontal Cortex in relation to future time perspective decision making. A study using VBM to investigate procrastination found that grey matter volumes within these areas negatively correlated with procrastination scores and an individual's future time perspective (Liu, & Feng, 2019). A supportive study (Schacter & Addis, 2009) has also shown both the Parahippocampal Gyrus and medial temporal lobe (encompassing both Parahippocampal and Hippocampal regions) have been involved in the perception of future events. Hassabis, Kumaran, and Maguire (2007) using fMRI found that when subjects are asked to construct imaginary scenes in the future, activation was seen within an extended brain network involving the Hippocampus and Parahippocamus, Posterior Parietal Cortices and the vmPFC. The current study identified correlates with switching after punishments and grey matter reductions within both the Parahippocampal Gyrus and Medial Temporal Lobe. Given this, it would be reasonable to propose that grey matter reductions within these areas may impact overall future planning. Sun et al. (2018) also found negative correlations within the Medial Temporal Lobe, Insula and Superior Temporal Gyrus and increased switching frequency, regardless of preceding trial. Morphometric differences within these areas may result in differences relating to the effectiveness of future planning, resulting in increased tendencies to switch. Within the task (Sun et al., 2018), participants were instructed to randomly guess in order to match the computers choice, which resulted in an average switch frequency of 43% in comparison to the computers 50% switching frequency. Thus, in Sun et al. (2018) if an individual switched more, they were more likely to be closer to the computers switching frequency, which would be an optimal overall strategy. This comparison may suggest neuroanatomical differences within the Temporal Lobe could be related to different strategies involving future planning which results in increased overall switching. Given, the results identified within Sun et al. (2018) were only related to switching regardless of previous trial outcomes, and the task used in the current study had no optimal strategy, further research is needed in order to further elucidate whether perception of the task as a whole, impacts an individual's likelihood to switch following a reward or loss.

Interestingly, the current study revealed associations between switching following punishment outcomes and lower grey matter volume within the Lingual Gyrus (Occipital lobe) and the Superior

Occipital Gyrus, areas which we had not predicted in our hypothesis. Currently, it is not clear as to why we may see lower grey matter volumes within this region that are associated with switches after punishment. One explanation is that it could be due to a network involved within this type of decision making. The Neurosynth findings suggest that both these areas show strong meta analytic coactivation between the cingulate cortex, which could be indicative of the cinglo-operculium network, which may be associated with tracking the previous outcomes of decisions (Dosenbach et al., 2007). Moreover, another study investigating the functional correlates of reward and loss processing using HCP data on a large sample, found activation within the Occipital cortex in relation to both reward and loss outcomes (Van de Streen et al., 2020). Thus, this result could be due to the increased power within the current study (Button et al., 2013). More research is needed to further investigate the role of the occipital cortex in relation to switches following punishment outcomes.

In order to better understand the association between the brain regions identified within the VBM analysis, a Neurosynth coactivation meta-analyses was conducted for each region. Once collated within MRIcroGL, the results revealed strong meta-analytic coactivation within the Insula for five of the six clusters identified within the VBM analysis, excluding the Superior Occipital Gyrus. The strong meta analytic coactivation seen within the Insula and other areas may suggest the involvement of a decision making network associated with switching, with the Insula being heavily involved in this process. The Insula has previously been identified as a potential hub which is involved in other large scale brain networks, such as; the salience network, a network which may be implicated in the generation of appropriate behavioural responses to external stimuli (Menon & Uddin, 2010). Moreover, Menon & Uddin (2010) proposed that the Insula provides a bottom up signal to the Anterior Cingulate when the consequence of a decision is negative. Coactivations of the Anterior Cingulate Cortex, another important region within the salience network, and an area previously associated with loss aversion (Tom, Fox, Trepel, & Poldrack, 2007), were also seen in relation to the Left Superior Temporal Gyrus and the Left Superior Occipital Gyrus. We therefore speculate that the Insula may be heavily implicated in a network of decision making that is associated with switching behaviour. It is important to note that structural studies and functional studies do not always overlap as the size of a brain region does not necessarily relate to its function or efficiency. Although research is progressing in order to create both structural and functional connection maps of brain networks, the role that function plays in cortical thickness is still unclear (Honey, Thivierge & Sporns, 2010). Therefore, further investigations are required, potentially using a combination of neuroimaging methods, to better understand the networks involved in this type of decision making.

6.1: Strengths and limitations

In order to measure switching, the current study adapted an fMRI reward paradigm developed by Delgado et al. (2000). Although we found structural differences that may be related to future thinking, more specifically located within the Medial Temporal Lobe and Parahippocampal Gyrus (Andrews-Hanna et al., 2010; Buckner, Andrews-Hanna & Schacter 2008; Andrews-Hanna, Smallwood & Spreng, 2014) the task did not give the participants an optimal strategy for task completion. The reward paradigm was adapted to suit the current study in order to measure switching after rewards compared with switching after losses, which may explain why the current study found no differences relating to general switching behaviour. Giving individuals incentive to be able to maximise rewards rather than just offering a 50% probability ratio on either option, could potentially lead to increased task involvement and task attention, and may lead to differing results than those found within the current study. Therefore, a task that is specifically designed to measure switching, such as the one used in Sun et al. (2018) may be a more comprehensive measure of switching behaviour. It is important to note, for selection of the current task we were limited to the data held within the HCP dataset. The amount of trials used within the current study may be another reason for differences in results. Delgado et al. (2000), conducted their study on a total of 190 trials utilising the reward paradigm, whereas in the current study, only 58 were included in the analysis due to the time constraints associated with conducting a study on a large sample. Consequently, future studies could increase time on the task and measure the effect this has on responses to switches after either rewards or punishments. It is important to note, for selection of the current task we were limited to the data held within the HCP dataset. Although, task differences may play a role in the differing results, this is unlikely to have a high impact on the results as these disadvantages were outweighed by the advantages of using a large sample size, which may provide another explanation for the disparate results found within the current study.

Studies that have used large samples to replicate findings from smaller have often found different results. In a study investigating delay discounting, Owens et al. (2017) found significant correlations within the Bilateral Middle Temporal Gyrus and Bilateral Entorhinal Cortex on a sample size of 1113 subjects. However, they did not find any differences within areas identified in studies with small sample sizes such as Right Orbitofrontal Cortex, Right Anterior Cingulate (Cho et al., 2013; Mohammadi et al., 2016; sample sizes: 34 and 70 respectively). An advantage of the current study is that it was conducted on a large cohort of healthy individuals, given the majority of previous studies have investigated the impact of rewards and losses on healthy participants versus individuals with behavioural addictions (Moreno-López et al., 2012; Koehler et al., 2015; Mohammadi et al., 2016). A possible explanation accounting for differing results found by Owens et al. (2017) may be due to

cognitive impulse control (Cho et al., 2013). Considering that both the current study and the study conducted by Owens et al. (2017) utilised a large cohort of healthy individuals, this could also provide an explanation of the results found in the current study as we did not see any structural differences in relation to reward switches. Individuals who tend to be more impulsive could show increased grey matter within this area as they have to exert more effort to be able to control impulses than healthy individuals (any individual that does not show signs of addictive behaviours, disease or dysfunction).

To analyse the association between grey matter volumes and switching, the current study used VBM analyses. Although VBM is a widely used technique in measuring structural differences, there are certain problems with the use of the method that can arise. The first of which is smoothing kernel size, as previous studies have shown that using a different kernel can influence how the method detects atrophy from statistical maps (Shen, Szameitat & Sterr, 2007). Using different kernel sizes on studies with smaller samples can vastly affect the results. A strength of the current study, is the use of a high sample size, resulting in the mitigation of any errors within this stage of the VBM process. The current study utilised a kernel size of 8mm, a recommended kernel size for a study of this nature. However, according to the study conducted by Shen and Sterr (2013), using a smaller kernel may yield different results, therefore future studies should investigate this by using a kernel of 6mm or less, as to our knowledge, this has not previously been investigated. Ultimately, due to the high sample size in the current study, errors that occur within the VBM analysis on smaller sample sizes are slightly mitigated, resulting in the study providing a valuable and valid addition to current literature investigating the relationship between VBM and decision making

6.2: Future Directions

Given some of the limitations identified above, future research could employ a task that is specifically designed to measure switching such as the random card guessing task utilised in Sun et al. (2018) study, in order to further investigate the impact the outcome of a previous decision has on future decision making, and the relationship with neuroanatomy. In addition, there is room for further progress in determining the involvement of the Insula as it remains unclear as to why this area was heavily involved in switching after punishments but not after rewards. Moreover, future studies could investigate how individual differences in circumstance, differing moods and individual values, affect how an individual reacts to either a reward or loss, and how this impacts future decision making strategies.

In this study, we performed a VBM analysis to investigate associations between whole brain grey matter volumes and frequency of switching following reward trials, in comparison to frequency of

switches following loss trials. The results revealed weak negative correlations between increased tendencies to switch following punishment trials and grey matter volumes within the Left Superior Temporal Gyrus, Left Lingual Gyrus, Medial Occipital Lobe, Left Superior Occipital Gyrus, Right Insula, Right Middle Temporal Gyrus and Left Parahippocampal Gyrus. The significant correlation between punishment switches and reduced Insula volume may be a result of a unique effect causing individuals with lower grey matter volume to behave differently following receipt of a punishment. Another significant finding was overall, individuals switched more after rewards in comparison to losses. Both these findings suggest the outcome of a previous trial may directly influence the decision to switch, providing new insights into the effects that a previous decision can have on subsequent choices. However, the extent to which these structural differences affect neural processing relating to future decision making remains unresolved due to the weak associations between grey matter volume and switching, and may benefit from future studies using a combination of neuroimaging methods to further understand the neural underpinnings of decision making based on the receipt of a previous reward or loss.

This study differs from prior investigations in two principle aspects. First, it assesses an individual's tendency to switch based on previous reward or loss outcomes, building on the work of Sun et al. (2018). Second, the study is conducted on a large sample size of healthy individuals. Our findings highlighting the Insula, an area previously associated with the integration of emotions within decision making processes, provide further support for prior investigations of loss aversion suggesting structural differences within this region may be strongly associated with how an individual processes a loss. Our findings also have the potential to further improve our understanding of the relationship between brain structure and decision making, highlighting individual differences relating to how healthy individuals respond after the impact of a prior reward or loss.

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Appendix

Appendix A – preregistration

Examining neuroanatomical correlates of switch behaviour following rewards and losses: a voxel-based morphometry study

Matt Westerman, Glyn Hallam & Chris Retzler

Background

Functional neuroimaging studies have demonstrated the role of areas such as the striatum and the frontal Cortex in the differential processing of rewards and punishments (Delgado et al., 2000). Structural analyses suggest that grey matter volume in these areas may be linked with disorders such as pathological gambling (Koehler, Hasselmann, Wüstenberg, Heinz & Romanczuk-Seiferth, 2015; Mohammadi et al., 2016). However, very little research has looked at the relationship between brain structure and the effect of rewards and punishments on subsequent choices in healthy individuals.

This study will utilise a large secondary dataset (Human Connectome Project) which includes an adapted version of the task used by Delgado et al. (2000) in which participants are asked to guess whether the value of a card will be higher or lower than five. The aim is to investigate the effects of monetary wins and losses on subsequent choices, and whether these choices correlate with anatomical volume of relevant brain areas.

Within lab-based gambling tasks, losses have been shown to motivate individuals to switch response (e.g. Knutson et al., 2003) or to stop gambling (e.g. Campbell-Meiklejohn, Woolrich, Passingham & Rogers, 2008). Similarly, an fMRI study demonstrated that losses were more likely to result in risky decisions and that this was positively correlated with increased activation in the frontoparietal

network and left lateral orbitofrontal Cortex, and negatively correlated with activation in the amygdala and the caudate nucleus (Xue, Lu,

Levin & Bechara, 2011). However, it is less clear how wins and losses motivate participants' choices, to stick or switch response and whether these strategies are related to brain anatomy.

To address this question, a recent voxel-based morphometry (VBM) study investigated the relationship between grey matter volume and switching behaviour (Sun et al., 2018). In a binary choice game, a greater likelihood of switching behaviour was associated with increased grey matter volume in brain areas including the frontal pole, posterior cingulate Cortex, and left Insula, and with reduced grey matter volume in the medial temporal lobe and right Insula. However, this study did not look at differences that might have been driven by the outcome of the previous trial (i.e. a win or a loss). We therefore aim to extend this finding utilising a large open-access dataset (Human Connectome Project) to see if grey matter volume relates to switching behaviour following a win or a loss.

Hypotheses

1. As in Sun et al. (2018), there will be a significant positive correlation between grey matter volume of the frontal pole, posterior cingulate, and left Insula and the tendency to switch behaviour in the gambling task (regardless of preceding trial).
2. As in Sun et al. (2018), there will be a significant negative correlation between grey matter volumes of the medial temporal lobe and right Insula Cortex in relation to switching frequency (regardless of preceding trial)
3. Grey matter volumes will be associated with frequency of switching after loss trials (punishment) compared to win trials (reward).

Explanation of existing data

This study will utilise data collected by the Human Connectome Project (Van Essen et al. HCP, 2013). This open source dataset includes T1 structural MRI scans, demographic and behavioural data for 1113 participants (aged 22-35). Participants were medically assessed and had no significant history of psychiatric disorder, neurological disorders, cardiovascular disease or Mendelian genetic disease.

Reward paradigm

In order to assess participant's responses to rewards and losses, we will be using an adapted version of Delgado et al. (2000) reward paradigm. In this study, participants were asked to guess whether the value of a card is higher or lower than five.

Trials began with a question mark (presented for up to 1500 ms) indicating that participants had to make a guess between 1 and 9. For every successful prediction the participant gained $1 (reward) and lost $0.50 (loss) for every unsuccessful prediction. In order to make the predictions participants were given two buttons to respond; the first button indicating a guess greater than 5 and the second button indicating a value lower than 5. There were three types of trials in the experiment, reward

trials to which the participant were rewarded $1, loss trials where they lost $0.50 and neutral trials where the number 5 would appear and participants did not gain or lose any reward. The outcome of each trial was predetermined as a reward, punishment or neutral event. The feedback was presented for 1000 ms, followed by an intertrial interval in which a fixation ("+") was presented for 1000 ms.

The task was presented in blocks of 8 trials that were either mostly reward or mostly loss, but still contained a mix of trial types. In each of the two runs there were two mostly reward and two mostly loss blocks interleaved with four fixation blocks (duration 15 sec). Each participant completed a total of 62 trials.

Structural MRI data collection procedure

Structural MRI scans were acquired using a customised Siemens 3.0 T "Connectome Skyra" (Siemens AG, Erlanger, Germany) using a 32-channel head coil. Two separate averages of the T1-weighted image were acquired using 3D, gradient echo pulse sequence (MPRAGE) with a resolution of 0.7 mm3 isotropic (FOV = 224 × 224, matrix = 320 × 320, 256 sagittal slices; TR = 2400 ms and TE = 2.14 ms). All scans have undergone quality assurance procedures as outlined in Marcus et al. (2013).

VBM pre-processing

In order to analyse grey matter volumes, we will use Voxel based morphometry (VBM). The data will be pre-processed using statistical parametric mapping software (SPM12; Wellcome Department of Cognitive Neurology, London, UK, https://www.fil.ion.ucl.ac.uk/spm/) implemented in Matlab (Mathworks Inc., Natick, MA). T1 weighted images will be segmented into grey matter, white matter and cerebrospinal fluid using an extension of the standard unified segmentation model in SPM12. Grey matter will then be normalised to Montreal Neurological institute (MNI) standard space generating template images and flow fields.

Grey matter segmentations will be spatially normalised across all participants using the

DARTEL algorithm (Diffeomorphic Anatomical Registration Through Exponentiated Lie

Algebra) voxel size: 1.5 mm × 1.5 mm × 1.5 mm in MNI space. The data will then be smoothed with a 8mm FWHM (full width half maximum) Gaussian filter. Images will then be modulated to create Jacobian scaled grey matter images using deformations estimated in the previous step.

Measured variables

Whole brain VBM analysis (grey matter density and concentration will be analysed) will be conducted on T1 weighed images. Further region-of-interest analyses may be carried out for areas identified as having a priori interest.

Switching behaviour will be measured by the following three outcomes; percentage of switches following reward trials, percentage of switches following loss trials, and overall percentage switches.

Statistical models

In order to identify which regions play a role in switching behaviour dependent on prior trials, a full factorial design will be used in SPM12 in order to conduct a multiple regression analysis. Whole-brain statistical analysis will be performed on normalized and smoothed grey matter maps using SPM12. In order to assess how this uniquely contributes to switching behaviour, percentage of switches after rewards and percentage of switches after losses will be entered into a regression model against total intercranial volume, age and gender. Further analysis will be conducted of any regions that show significance differences in relation to switching behaviours.

Data exclusion

Participants will only be included if they have complete behavioural data from the gambling task and a T1 structural MRI scan. Participants who show 100% response rate for either the higher or lower option will be excluded from the analysis due to task noncompliance as participants were instructed to guess on each trial. After exclusions, our dataset contains 889 participants.

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Appendix B - VBM pipeline settings

Pre-processing steps

Step 1: File conversion

Conversion of files into NIfTI format using check reg function. Display will be used to check the files have converted correctly

Step 2: Segmentation

Data:

- Channel- only need one channel as not T2 data
- Volumes: Number of scans to be segmented
- Bias regularisation: light regularisation (0.001)
- Bias FWHM: 60mm cutoff
- Save Bias Corrected: Not needed yet

Tissue 1

Tissue: Grey matter

- Tissue probability map: Located in SPM programme files
- Num. Gaussians: 1
- Native Tissue: Native + Dartel imported.
- Warped Tissue: None

Tissue 2

Tissue: White matter

- Tissue probability map: Located in SPM programme files
- Num. Gaussians: 1.
- Native Tissue: Native + Dartel imported.
- Warped Tissue: Leave at None.

Tissue 3

Tissue: Cerebrospinal fluid

- Tissue probability map: Located in SPM programme files
- Num. Gaussians: 2
- Native Tissue: Native Space
- Warped Tissue: None.

Tissue 4

Tissue: skull tissue.

- Tissue probability map: Located in SPM programme files
- Num. Gaussians: 3
- Native Tissue: None.
- Warped Tissue: None.

Tissue 5

Tissue: soft tissue outside the brain (meningocele)

- Tissue probability map: Located in SPM programme files
- Num. Gaussians: 4
- Native Tissue: None.
- Warped Tissue: None.

Tissue 6

Tissue: Extraneous factors (air around the head)

- Tissue probability map: Located in SPM programme files
- Num. Gaussians: 2
- Native Tissue: None.
- Warped Tissue: None.

Warping & MRF

- MRF Parameter: 1
- Clean Up: Light clean
- Warping regularisation: 1x5 double
- Affine regularisation: ICBM space template- European brains?
- Smoothing: 0mm
- Sampling distance: 3
- Deformation fields: None

Step 3: Run DARTEL to create templates

Images

- Images: Imported grey matter images
- Images: imported white matter images

Settings

- Template basename: template
- Regularisation form: Linear Elastic energy

Outer iteration: New: Outer iteration

- Inner iteration: 3

- Reg Params: 4 2 1e-06
- Time steps: 1
- Smoothing Parameter: 16

Outer iteration 2

- Inner iteration: 3
- Reg Params: 2 1 1e-06
- Time steps: 2
- Smoothing Parameter: 8

Outer iteration 3

- Inner iteration: 3
- Reg Params: 0.5 0.25 1e-06
- Time steps: 4
- Smoothing parameter: 2

Outer iteration 4

- Inner iteration: 3
- Reg Params: 0.25 0.125 1e-06
- Time steps: 16
- Smoothing parameter: 1

Outer iteration 5

- Inner iteration: 3
- Reg Params: 0.25 0.125 1e-06
- Time steps: 64
- Smoothing parameter: 0.5

Outer iteration 6

- Inner iteration: 3
- Reg Params: 0.1 0.01 0.001
- Time steps: 64
- Smoothing parameter: 1

Optimisation settings

- LM Regularisation: 0.01
- Cycles: 3
- Iterations: 3

Step 4 Normalisation to MNI Space

MNI space

- Dartel template: using final template created in previous step
- Select according to: Many subjects
- Voxel sizes: 1.5x1.5x1.5
- Bounding Box: 2x3 double
- Preserve: preserve amount (modulation)
- Gaussian FWHM (8, 8, 8)

Step 5. Statistical analysis

Factorial design specification

Directory – create directory prior to analysis and select this

Design

- Multiple regression
- Scans: previously computed files selected
- Intercept: include intercept
  Covariates: new covariate- the plan will be to include covariates here
  Masking
  - Threshold masking: Absolute masking
  - Threshold: 0.2

Global calculation

- Globals (GM and WM) will be computed by adding the values in each image and multiplying by the volume of each voxel
- Total intercranial volume = GM + WM+ CSF. These will then be used within MATLAB.

Global normalisation

- Overall grand mean scaling: No
- Normalisation: proportional scaling

Appendix C – Virtual Basic Code

Code 1: VBA code to change name of T1 files to corresponding HCPID
(comments in green)

Note: In order for the code to be run, file locations were included within an excel document which this code extracted and utilised. The examples below are purely examples for the purposes of the thesis and cannot be run without this additional information.

```
Sub gett1file()

Dim myworkbook As String

myworkbook = "COde for t1"

Range("J1").Select

Do Until ActiveCell.Value = ""

directory = ThisWorkbook.Path & "\" 'uses files directory to identify file'

filetext = Selection.Value & ""

Filename = ActiveCell.Offset(0, 1) 'renames file to corresponding HCPID'
```

```
Name directory & filetext As directory & filetext & Filename
ActiveCell.Offset(1, 0).Select 'moves to next file'
Loop
End Sub
```

Code 2: VBA code to complete file reconciliation

```
Sub getfiles()
Dim oFSO As Object
Dim oFolder As Object
Dim oFile As Object
Dim i As Integer
 Set oFSO = CreateObject("Scripting.FileSystemObject")
 Set oFolder = oFSO.GetFolder("D:") 'insert folder to find'
 For Each oFile In oFolder.Files
 Cells(i + 1, 1) = oFile.Name
 i = i + 1
Next oFile 'Returns filenames within an Excel document'
End Sub
```

Code 3: Example of VBA code to extract and save behavioural data

```
Sub behfilechangecode()
Dim path1 As String
Dim path2 As String
Dim myrow As String
myrow = ActiveCell.Row 'extracts filename from excel doc template'
Dim filename As String
path1 = "D:\Filename\"
myfilename = ActiveCell.Value
path1 = "D:\HCP\filename\MNINonLinear\Results\tfMRI_GAMBLING_RL\GAMBLING_run1_TAB.txt"
Range("A1").Select
Do Until ActiveCell.Value = ""
```

```
Workbooks.OpenText
filename:="D:\HCP\myfilename\MNINonLinear\Results\tfMRI_GAMBLING_RL\GAMBLING_run1_TA
B.txt", _

DataType:=xlDelimited, Tab:=True

ActiveWorkbook.SaveAs filename:="D:\filename \myfilename_1.xlsx"

Workbooks.OpenText
filename:="D:\HCP\myfilename\MNINonLinear\Results\tfMRI_GAMBLING_LR\GAMBLING_run2_TA
B.txt", _

DataType:=xlDelimited, Tab:=True

ActiveWorkbook.SaveAs filename:="D:\filename\myfilename_2.xlsx"

ActiveSheet.ActiveCell.Offset (1,0 ).select

Loop

End Sub
```

Appendix D: SPSS Descriptive statistics output.

```
NEW FILE.
DATASET NAME DataSet1 WINDOW=FRONT.
DESCRIPTIVES VARIABLES=Switchafterrewards Switchafterpun
  /STATISTICS=MEAN STDDEV MIN MAX.
```

Descriptives

Notes

Output Created		14-APR-2020 11:33:27
Comments		
Input	Active Dataset	DataSet1
	Filter	<none>
	Weight	<none>
	Split File	<none>
	N of Rows in Working Data File	851
Missing Value Handling	Definition of Missing	User defined missing values are treated as missing.
	Cases Used	All non-missing data are used.

Syntax		DESCRIPTIVES VARIABLES=Switchafterrewards Switchafterpun /STATISTICS=MEAN STDDEV MIN MAX.
Resources	Processor Time	00:00:00.00
	Elapsed Time	00:00:00.00

[DataSet1]

Descriptive Statistics

	N	Minimum	Maximum	Mean	Std. Deviation
Switchafterrewards	851	0	25	11.76	4.895
Switchafterpun	851	1	25	11.17	4.167
Valid N (listwise)	851				

T-TEST PAIRS=Switchafterrewards WITH Switchafterpun (PAIRED)

/CRITERIA=CI(.9500)

/MISSING=ANALYSIS.

T-Test

Notes

Output Created		14-APR-2020 11:34:13
Comments		
Input	Active Dataset	DataSet1
	Filter	<none>
	Weight	<none>
	Split File	<none>
	N of Rows in Working Data File	851
Missing Value Handling	Definition of Missing	User defined missing values are treated as missing.
	Cases Used	Statistics for each analysis are based on the cases with no missing or out-of-range data for any variable in the analysis.
Syntax		T-TEST PAIRS=Switchafterrewards WITH Switchafterpun (PAIRED) /CRITERIA=CI(.9500) /MISSING=ANALYSIS.
Resources	Processor Time	00:00:00.00
	Elapsed Time	00:00:00.00

Paired Samples Statistics

		Mean	N	Std. Deviation	Std. Error Mean
Pair 1	Switchafterrewards	11.76	851	4.895	.168
	Switchafterpun	11.17	851	4.167	.143

Paired Samples Correlations

		N	Correlation	Sig.
Pair 1	Switchafterrewards & Switchafterpun	851	.250	.000

Paired Samples Test

		Paired Differences					t	df	Sig. (2-tailed)
					95% Confidence Interval of the Difference				
		Mean	Std. Deviation	Std. Error Mean	Lower	Upper			
Pair 1	Switchafterrewards - Switchafterpun	.597	5.580	.191	.222	.972	3.121	850	.002

```
MEANS TABLES=rew pun BY gen
  /CELLS=MEAN COUNT STDDEV.
```

Means

Notes

Output Created		03-FEB-2021 18:45:07
Comments		
Input	Active Dataset	DataSet1
	Filter	<none>
	Weight	<none>
	Split File	<none>
	N of Rows in Working Data File	873
Missing Value Handling	Definition of Missing	For each dependent variable in a table, user-defined missing values for the dependent and all grouping variables are treated as missing.
	Cases Used	Cases used for each table have no missing values in any independent variable, and not all dependent variables have missing values.
Syntax		MEANS TABLES=rew pun BY gen /CELLS=MEAN COUNT STDDEV.
Resources	Processor Time	00:00:00.02
	Elapsed Time	00:00:00.00

Case Processing Summary

	Cases					
	Included		Excluded		Total	
	N	Percent	N	Percent	N	Percent
rew * gen	851	97.5%	22	2.5%	873	100.0%
pun * gen	851	97.5%	22	2.5%	873	100.0%

Report

gen		rew	pun
female	Mean	12.00	11.70
	N	461	461
	Std. Deviation	4.829	3.954
Male	Mean	11.48	10.54
	N	390	390
	Std. Deviation	4.962	4.327
Total	Mean	11.76	11.17
	N	851	851
	Std. Deviation	4.895	4.167

```
MEANS TABLES=rew pun BY age
  /CELLS=MEAN COUNT STDDEV.
```

Means

Notes

Output Created		03-FEB-2021 19:04:57
Comments		
Input	Active Dataset	DataSet1
	Filter	<none>
	Weight	<none>
	Split File	<none>
	N of Rows in Working Data File	873
Missing Value Handling	Definition of Missing	For each dependent variable in a table, user-defined missing values for the dependent and all grouping variables are treated as missing.
	Cases Used	Cases used for each table have no missing values in any independent variable, and not all dependent variables have missing values.
Syntax		MEANS TABLES=rew pun BY age /CELLS=MEAN COUNT STDDEV.
Resources	Processor Time	00:00:00.02
	Elapsed Time	00:00:00.00

Case Processing Summary

	Cases					
	Included		Excluded		Total	
	N	Percent	N	Percent	N	Percent
rew * age	851	97.5%	22	2.5%	873	100.0%
pun * age	851	97.5%	22	2.5%	873	100.0%

Report

age		rew	pun
22-25	Mean	11.35	10.40
	N	187	187
	Std. Deviation	5.152	4.493
26-30	Mean	11.57	11.07
	N	366	366
	Std. Deviation	4.943	4.160
31-35	Mean	12.26	11.76
	N	290	290
	Std. Deviation	4.643	3.909
36+	Mean	12.50	12.00
	N	8	8
	Std. Deviation	4.811	2.777
Total	Mean	11.76	11.17
	N	851	851
	Std. Deviation	4.895	4.167