Explaining Compulsive Hair-pulling Disorder (Trichotillomania) through the lens of Reinforcement Sensitivity Theory

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Abstract

Compulsive hair-pulling, also known as trichotillomania (TTM) is a debilitating chronic psychological disorder that typically involves the continued pulling out of individual hairs over a long period of time. Tension exists in the literature as to what motivates this behaviour. Typically, it is argued that varying levels of compulsivity, in response to punishment, and impulsivity, in response to reward are involved. The reinforcement sensitivity theory of personality (RST) captures the elements of reward and punishment and integrates them across various areas of enquiry: biological, psychological, and behavioural. The main argument of RST is that human behaviour arises from our response to rewarding and punishing stimuli leading to various behaviours classified by: the behavioural inhibition system - approach to punishing stimuli; the behavioural activation system - approach to rewarding stimuli; the fight flight freeze system - avoidance of punishing stimuli; and constraint – exerting psychological control over all systems.

These elements encapsulate the tension in the current TTM literature, and are argued to motivate the behaviour of hair-pulling. The overarching aim of this dissertation was to examine the relevance of RST to symptoms of TTM. The research employed a mixed method approach including: a qualitative exploration of the experiences of stimuli, motivation and constructs of the RST in TTM; a quantitative examination of the relationship between RST constructs and TTM; and exploration of underlying neurobiological mechanisms associated with TTM.

To better understand the behaviours and experiences of relevance to RST, in-depth semi structured interviews were conducted with a group of people meeting the DSM-5 criteria for TTM (n=16). Transcripts were subjected to theoretical thematic analysis to organise a rich and complex description of behavioural, emotional and cognitive responses to stimuli within a total of 30 themes and sub-themes. Rewarding stimuli, such as which hair to
pull, tended to be consciously chosen by the participant. However, rewarding life experiences more generally were met with suspicion and mistrust. Participants viewed themselves as innately and highly sensitive to punishment with avoidance behaviours dominating transcripts.

Two studies were then conducted to define avoidance behaviours, a central feature of the Fight, Flight, Freeze system, experienced by those with hair-pulling symptoms. Participants experienced a range of hair-pulling severity. Using two samples, study one included an exploratory factor analysis (n=278), and a confirmatory factor analysis (n=295) to identify five types of avoidance: avoidance of non-social goals, self-concealment, behavioural social avoidance, avoidance of relationship problems, and avoidance of thinking about the future. In the second study, a multivariate analysis of variance (n=300) demonstrated that those who experience hair-pulling symptoms experienced more avoidance on all five types relative to the control group.

The relationship between RST and TTM was further investigated over a series of three studies that used self-report questionnaires constructed to measure RST personality traits. Study one revealed higher sensitivity to reward and punishment between those with hair-pulling symptoms (n=89) and those without symptoms (n=206) when participants were recruited via the internet. Study 2 revealed that group membership, those with (n=25) and those without hair-pulling symptoms (n=25), could be predicted based on lower sensitivity to reward and punishment when recruited via the internet. Study 3 revealed that group membership between those who met the DSM 5 criteria for TTM (n=22) and healthy controls (n=22) could be predicted based on higher sensitivity to punishment and higher depression for those with TTM. Findings from the three studies indicate that sensitivity to punishment and sensitivity to reward contributes to hair-pulling behaviour at sub-clinical levels.
However, when the DSM 5 criteria are met sensitivity to punishment and depression become more important.

Before addressing the question of whether brain activation in response to reward differs between those with TTM and healthy controls, a systematic review of primary studies that used neuroimaging and neuropsychological tests was conducted. A search adhering to specified inclusion and exclusion criteria revealed a total of 215 records, 30 of which were included in a qualitative synthesis. Results from imaging studies revealed some differences between those with TTM and controls in the ventral striatum, caudate, amygdala, occipital lobe, cerebellum and frontal lobe, with correlations to hair-pulling severity inconclusive. The neuropsychological literature showed that divided attention, visual memory, working memory and automatic motor responses merit further investigation. Results of the review indicated many areas for further enquiry. The most pertinent being the relationship between the striatum involved in reward processing and TTM.

The striatum is part of the hierarchy of brain structures proposed to underlie the behavioural activation system and sensitivity to reward. A group experiencing TTM (n=15) and healthy controls (n=19) completed a gambling task during functional magnetic resonance imaging. Questionnaires measuring clinical symptoms and trait sensitivity to reward and punishment were also completed. Whole brain analysis revealed that those who experience TTM had higher activation of the striatum in response to reward (monetary gain) than controls. No differences were found in response to punishment (monetary loss). Results indicated that those with TTM experience reward processing abnormalities, which may be subjectively experienced as high sensitivity to punishment.
Implications for understanding and treating TTM, are discussed within the framework of the reinforcement sensitivity theory. A new model of understanding TTM is proposed based on the presented data, ‘the motivational model of trichotillomania’.
Declaration

I declare that this dissertation does not incorporate without acknowledgment any material previously submitted for a degree in any University, College of Advanced Education, or other educational institution, and that to the best of my knowledge and belief it does not contain any material previously published or written by another person except where due reference is made in the text. I further declare that the ethical principles and procedures specified in the Faculty of Health, Arts and Design Human Research Ethics Committee document have been adhered to in the preparation of this report. I warrant that I have obtained, where necessary permission from the copyright owners to use and third party copyright material reproduced in the thesis, or to use and of my own published work in which the copyright is held by another party.

Reneta Katie Slikboer
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First, I would like to thank my supervisors, Maja Nedeljkovic, Susan Rossell and David Castle who provided helpful support and guidance throughout the creation of this thesis. More specifically, their faith in my ability to excel in the face of challenges, and the invaluable insight and judgement that years of developing expertise in their respective fields offered. Maja and Susan who shared the role of principle supervisor were not only inspirational academic role models for me, they also stretched my academic abilities, interests and skills beyond what I thought were my limitations. Largely because of their presence I felt protected and knew my academic progress would continue despite a number of personal crises, and debilitating chronic pain.

I am also grateful to my colleagues with whom I share a love of learning and drive to understand what is not yet known. Some of whom deserve special mention: Jamie Byrne, Maree Reser, Imogen Rehm, Andrea Wallace, Matthew Hughes and Luke Smillie. Our collaboration, debates, discussions and sharing of resources consistently propelled the research forward. Without doubt sharing the journey made negotiating the post-graduate jungle an adventure full of excitement and surprise, rather than an obstacle to overcome. Thank you for fostering my passion in creating new knowledge.

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* = publication or funding directly associated with research herein

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Media


Miscellaneous


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**List of Common or Important Abbreviations**

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<th>Description</th>
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<tbody>
<tr>
<td>ANOVA</td>
<td>Analysis of variance</td>
</tr>
<tr>
<td>BAS</td>
<td>Behavioural activation system</td>
</tr>
<tr>
<td>BIS</td>
<td>Behavioural inhibition system</td>
</tr>
<tr>
<td>CFA</td>
<td>Confirmatory factor analysis</td>
</tr>
<tr>
<td>CBM</td>
<td>Comprehensive behavioural model of trichotillomania</td>
</tr>
<tr>
<td>DFA</td>
<td>Discriminate function analysis</td>
</tr>
<tr>
<td>EFA</td>
<td>Exploratory factor analysis</td>
</tr>
<tr>
<td>FFFS</td>
<td>Fight, Flight, Freeze system</td>
</tr>
<tr>
<td>fMRI</td>
<td>Functional magnetic resonance imaging</td>
</tr>
<tr>
<td>HPD</td>
<td>Hair-pulling disorder (trichotillomania)</td>
</tr>
<tr>
<td>MANOVA</td>
<td>Multi variate analysis of variance</td>
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<tr>
<td>MDD</td>
<td>Major depressive disorder</td>
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<tr>
<td>OCD</td>
<td>Obsessive compulsive disorder</td>
</tr>
<tr>
<td>SP</td>
<td>Sensitivity to punishment</td>
</tr>
<tr>
<td>r-RST</td>
<td>Revised Reinforcement sensitivity theory (2000)</td>
</tr>
<tr>
<td>RST</td>
<td>Reinforcement sensitivity theory</td>
</tr>
<tr>
<td>SR</td>
<td>Sensitivity to reward</td>
</tr>
<tr>
<td>TTM</td>
<td>Trichotillomania (hair-pulling disorder)</td>
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Note: This list contains only important or commonly used abbreviations mentioned within the text and is not exhaustive.
1 Introduction
1.1 Description of trichotillomania

An individual experiencing trichotillomania (TTM; hair pulling disorder) may compulsively pull out their hairs one at a time over an extended period (American Psychiatric Association, 2013). Hairs may be pulled from anywhere on the body, although the scalp is most common (Woods, Flessner, Franklin, et al., 2006a). High levels of distress and impairment are apparent. Distress can be experienced as shame, embarrassment, loneliness, depression and anxiety. Impairment is often psychosocial, typically a result of avoiding situations in which hair loss may be noticed, such as, swimming, job interviews, hairdressers and other public places (American Psychiatric Association, 2013; Rehm, Nedeljkovic, & Moulding, 2012; Woods, Flessner, Franklin, et al., 2006a).

Despite the term trichotillomania having been coined in 1889 (Hallopeau, 1889), progress in understanding the disorder has been slow. Even as late as 1992 there was scepticism regarding the validity of trichotillomania as a distinct disorder (Dean, Nelson, & Moss, 1992). It had been thought that hair pulling was symptomatic of other psychological disturbance and that hair pulling functioned to relieve underlying tension caused by comorbid disorders (Christenson, Mackenzie, & Mitchell, 1991; Dean et al., 1992). It is now understood that not all individuals with TTM experience tension when pulling (Woods, Flessner, Franklin, et al., 2006a) and the current diagnostic criteria in the diagnostic and statistical manual of mental disorders – fifth edition reflects this (American Psychiatric Association, 2013).

TTM is a disorder noted within the Obsessive Compulsive and Related Disorders diagnostic group. In addition to pulling out hair resulting in hair loss, diagnostic criteria are: repeatedly attempting to decrease or stop pulling; hair pulling creates clinically significant distress or impairment in social, occupational, or other important areas of life; the hair
pulling or loss is not due to another medical condition; and hair pulling is not better
explained by another mental disorder (American Psychiatric Association, 2013).

Hairs may be pulled from anywhere on the body. Pulled areas in decreasing order of
prevalence are: scalp, brows, lashes, pubic, legs, arms, armpits, trunk, moustache and beard
(Woods, Flessner, Franklin, et al., 2006a). The disorder is not age specific but can appear in
infancy with spontaneous recovery in early childhood. More often hair pulling begins during
early puberty. Women with TTM tend to show more general impairment and have earlier
onset of symptoms than men. However, men tend to exhibit more comorbid obsessive
compulsive disorders and tics. TTM is typically chronic, with severity fluctuating over time.
Average duration of TTM is 21 years (American Psychiatric Association, 2013; Christenson
et al., 1991; Lochner, Seedat, & Stein, 2010).

TTM may affect all areas of life. Particularly distressing are sexual encounters and
visits to the hair dresser (Bloch, 2009; Stemberger, Stein, & Mansueto, 2003; Stemberger,
Thomas, Mansueto, & Carter, 2000; Woods, Flessner, Franklin, et al., 2006b). TTM has a
pervasive influence on one’s life regardless of socioeconomic status. Individuals
experiencing TTM are found amongst the unemployed, students, and those who hold highly
desired jobs and positions (Cohen et al., 1995). Hair pulling may be isolated to waking hours
or during sleep, or both (Murphy, Redenius, Neill, & Zallek, 2007). Individuals go to great
lengths to cover up hair loss involving much time and money, and may use tobacco and
alcohol to cope with urges and negative feelings (American Psychiatric Association, 2013;
Flessner et al., 2008; Woods, Flessner, Franklin, et al., 2006a).

Negative feelings such as shame, irritability and feeling unattractive are common with
TTM, and these feelings are associated with lack of control and low self-esteem
(Arabatzoudis, Rehm, Nedeljkovic, & Moulding, 2017; Casati, Toner, & Yu, 2000;
Stemberger et al., 2000). These elements affect one’s environment including relationships. Frequent arguments and keeping secrets from loved ones are common (Stemberger et al., 2000). High rates of comorbidity are common in TTM, particularly depression and anxiety (Diefenbach, Mouton-Odum, & Stanley, 2002).

![Figure 1.1 Example of hair loss due to trichotillomania; Shukla, 2017](image)

### 1.2 Prevalence

One of the earliest investigations into the prevalence of TTM was an estimation based on nail biting. Hair-pulling was estimated at 10% life time and 4% point prevalence
(Azrin & Nunn, 1977). Twelve years later, prevalence estimates of trichotillomania were explored in an undergraduate student cohort. A questionnaire designed to detect a range of habits was used; the DSM criteria was not used and participants judged the severity of hair pulling symptoms on a scale that ranged from zero - no problem, to four - severe. Twenty two percent of the cohort reported a habit of pulling out hairs more than twice a month (Hansen, Tishelman, Hawkins, & Doepke, 1990). Of the total sample, 3.2% rated hair pulling as a severe problem and 7.9% rated the severity of hair pulling between moderate and severe.

The more stringent classification criteria from the DSM-III-R reduced the life time prevalence estimate from 3.2% (Hansen et al., 1990) to 0.6% amongst college students, inclusive of women and men (Christenson, Pyle, & Mitchell, 1991). A later estimation of 11% of college students and 4% of the general public was made when reasons for pulling were included in the hair-pulling criteria (Graber & Arndt, 1993). These results support Rothnaum, Shaw, Morris, & Ninan, (1993) who found a 10% prevalence in a student cohort. Interestingly only 2% of those found hair pulling distressing and only 1% experienced the combination of hair pulling, hair loss and distress. Research which examined the general population found that many people that experienced TTM did not have an official diagnosis. Only 40% of participants out of 123 had an official diagnosis, and 58% reported having no treatment (Cohen et al., 1995).

Early investigations into sex differences found TTM to be more common in men (25.8%) than women (20.8%) in a group of university students (Hansen et al., 1990). A subsequent study reported the reverse with TTM being more common in females 1.5% versus 3.4% (Christenson, et al., 1991). Rothnaum et al., (1993) also documented a tendency for more women than men to experience the condition which was supported by further research. Stanley, Borden, Bell, & Wagner, (1994) found that 80% of a college student
sample that pulled hair were women. Overall 15% of the total sample reported pulling hair, however less than 1% reported pulling for non-grooming purposes once a day or more.

Epidemiological research is needed into TTM in the general population, (Diefenbach, Reitman, & Williamson, 2000), as noted by Duke, Keeley, Geffken, & Storch, (2010) most prevalence estimates were based on cohorts of college or university students. The need for an epidemiological investigation is evidenced by the fact that TTM is found in other cultures: African American (Neal-Barnett, Statom, & Stadulis, 2011); Brazilian (Ferrão, Almeida, Bedin, Rosa, & D’Arrigo Busnello, 2006; Lovato et al., 2012); Japanese (Oguchi & Miura, 1977; Takei, 2000); Israeli (King et al., 1995); Chinese (Hon, Leung, & Ng, 2008).

Over the course of prevalence research into TTM a pattern has emerged whereby estimates fluctuate according to the criteria used, with more rigorous and restrictive criteria producing smaller estimates. A notable change over the history of epidemiological research into TTM is that the more recent the estimate, the more likely it is that women experience non-grooming related hair pulling than men. The consistent use of student populations in prevalence studies gives us exactly that, prevalence estimates of TTM only of that age group, not of TTM in childhood or late adulthood. Childhood and late adulthood TTM prevalence estimates are virtually non-existent despite the wide range of onset age.

1.3 Course and age of onset

Infant hair pulling may be considered normal tactile exploration (Tay, Levy, & Metry, 2004). However, TTM has been identified in children (American Psychiatric Association, 2013; King et al., 1995; Tay et al., 2004), from ages 3 - 6 years, it is typically less severe than in adults, has a better response to treatment and is more likely to
spontaneously remit. Not all children with a diagnosis of TTM go on to experience adult TTM (Bruce, Barwick, & Wright, 2005; Swedo & Rapoport, 1991). Response prevention as a treatment has been recommended for children 0 – 7 years of age, and habit reversal therapy for children older than 7 years (Bloch, 2009). When onset occurs in early puberty, symptoms are more likely to continue into adulthood with onset at this time most common (American Psychiatric Association, 2013; Swedo & Rapoport, 1991; Tay et al., 2004).

Most age of onset estimates are based on reports from adult cohorts, in studies that did not make a distinction as to whether childhood TTM was separate from the current experience of TTM as an adult. Average age of onset has been reported as 10 years (Cohen et al., 1995) and 14 years old (Lochner et al., 2010). No difference in severity or comorbidity have been found between individuals who began pulling before or after 14 years of age (Lochner et al., 2010). Age of onset has been discounted as being a useful predictor of prognosis, although sex can be of use. Women tend to have earlier onset of symptoms than men, approximately 13 years versus approximately 20 years respectively, and women tended to experience a longer duration of symptoms, 20 years versus 15 years respectively (Du Toit, Van Kradenburg, Niehaus, & Stein, 2001; Lochner et al., 2010). Despite the common perception that TTM fluctuates in severity, there is no empirical evidence to support the idea of periodic reductions or absence of symptoms. The data presented clearly demonstrates that TTM is most often a chronic disorder with onset commonly occurring in early puberty.

1.4 Hair pulling sites

Where hair grows on the body, it can be pulled out. How often a pulling location is targeted differs according to sex (Lochner et al., 2010). A larger portion of women,
approximately 89%, versus men, approximately 50%, pull from the scalp (Du Toit et al., 2001; Lochner et al., 2010), which may be a product of societal expectations (Casati et al., 2000). Women prefer to pull from the crown whereas men tend to pull from the left and right temple regions (Du Toit et al., 2001; Lochner et al., 2010). Other areas in which pulling occurs to varying degrees are the eyebrows, eyelashes, stomach and back, moustache and beard, arms and legs, and the pubic region (Du Toit et al., 2001; Lochner et al., 2010). The same locations have been identified in a nonclinical sample (Stanley et al., 1994). Pulling from the scalp, pubic region and eyes are the most common sites (Woods, Flessner, Franklin, et al., 2006a). Pulling from areas of the body are summarised in table 1.1 below.

<table>
<thead>
<tr>
<th>Pulling site</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Scalp</td>
<td>28% to 89%</td>
</tr>
<tr>
<td>Pubic region</td>
<td>28% to 50%</td>
</tr>
<tr>
<td>Eye brows</td>
<td>21% to 56%</td>
</tr>
<tr>
<td>Eyelashes</td>
<td>17% to 51%</td>
</tr>
<tr>
<td>Stomach and or back</td>
<td>6% to 8%</td>
</tr>
<tr>
<td>Chest</td>
<td>4%</td>
</tr>
<tr>
<td>Arm pits</td>
<td>12%</td>
</tr>
<tr>
<td>Moustache and or beard</td>
<td>4% to 20%</td>
</tr>
<tr>
<td>Arms and or legs</td>
<td>7% to 21%</td>
</tr>
<tr>
<td>Fingers</td>
<td>1%</td>
</tr>
</tbody>
</table>

Note: percentages taken from; Christenson et al., 1991; Du Toit et al., 2001; Lochner et al, 2010; Woods, Flessner, Franklin, et al., 2006.

1.5 Styles and sub-types of hair pulling

A focused pulling style and automatic pulling style have been identified as two subtypes (Flessner, Woods, Franklin, Cashin, & Keuthen, 2007). Focussed hair pulling
occurs when the individuals’ attention is focused on the hair pulling behaviour; the individual actively searches for a hair to pull; the behaviour has a compulsive quality to it. Automatic hair pulling occurs when the behaviour of hair pulling is outside of the individuals’ awareness and may be performed while doing other inactive activities such as reading, driving or using the phone (Christenson & Mackenzie, 1994). Those who pull with a more focused style tend to experience more shame. Interestingly, demographic characteristics and comorbidity do not differ between pulling styles. However, individuals who report experiencing both focused and automatic types of pulling styles equally, had poorer performance at school and work when compared to those who pulled hair predominantly in one style (Flessner, Conelea, et al., 2008; Lochner et al., 2010). Less than 0.01% experience exclusively one of these two styles (Flessner, Conelea, et al., 2008).

There exists tension in the literature as to whether ‘focused’ and ‘automatic’ styles of pulling are accurate descriptions of subtypes. They were proposed based on an exploratory (n = 848) and subsequent confirmatory (n = 849) factor analysis of data collected via the internet (Flessner et al., 2007). A replication study using a clinical sample (n = 193) failed to support the idea of focused and automatic styles of pulling in an exploratory factor analysis (Keuthen, Tung, Woods, et al., 2015). Rather than categories based on level of awareness, styles of pulling were reconceptualised as ‘intention’ and ‘emotion’. ‘Intention’ was proposed to measure the level of intent to pull hair, and ‘emotion’ was proposed to measure the degree to which negative emotions are experienced during pulling (Keuthen, Tung, Woods, et al., 2015). Correlational analyses support the separation of ‘intention’ and ‘emotion’ as two different pulling styles (Keuthen, Tung, Woods, et al., 2015).

Styles of hair pulling require further identification and description, as consistency and replication has not been demonstrated in the literature. While preliminary types of hair pulling – ‘focused’, ‘automatic, ‘intention’ and ‘emotion’- have been hypothesised as
relevant to treatment approaches, the relationship between pulling styles and therapeutic outcomes has not been tested. There is limited evidence supporting other sub-types of TTM, such as; positive vs. negative affective cues for pulling, hair pullers with vs. without OCD, and hair pullers with vs. without tics (Du Toit et al., 2001). Should future research solidify and confirm specific types of pulling styles, a dimensional conceptualization has been recommended (Lochner et al., 2010).

1.6 Heritability

Research has consistently indicated that genetics and heritability have a role in the aetiology of TTM. A recent study exploring familial TTM found that 8 of 128 first-degree relatives of those who have TTM, also experience TTM (Keuthen, Altenburger, & Pauls, 2014). Consistent with earlier research (Christenson, MacKenzie, & Reeve, 1992; Lenane et al., 1992), no individuals were found with TTM in the control group, the comparable difference was statistically significant (Keuthen et al., 2014). This is in line with research demonstrating that monozygotic twins were more likely to share a diagnosis of TTM (38.1%) versus dizygotic twins 0%. A heritability estimate was proposed between 76% and 78% depending on the diagnostic criteria (Novak, Keuthen, Stewart, & Pauls, 2009).

OCD was also found to have a genetic component linked to TTM (Keuthen et al., 2014). Relatives of those with TTM have a higher risk of developing OCD which leads to the argument that TTM and OCD are etiologically related. It was further proposed that there might be a familial sub-type of TTM that is comorbid with OCD (Keuthen et al., 2014). The proposal of a TTM + OCD familial sub-type stems from earlier work in which higher than expected rates of OCD were found in first-degree relatives of those with TTM; 19% of those with TTM had a family member who also met criteria (Lenane et al., 1992). Indeed, the
parents of children with TTM have also found to frequently experience tics, habits and OCD type symptoms (King et al., 1995; Schlosser, Black, Blum, & Goldstein, 1994).

The familial grouping and experience of TTM may be explained by the identification of specific genetic markers. The SLITRK1 gene has been implicated in TTM related disorders (Zuchner et al., 2006). Two different but closely situated sequence changes have been found in SLITRK1 that exist in families with one or more people diagnosed with TTM; i.e., changes in how amino acids argine, lysine, serine and glycine are ordered in the protein. It was suggested that this change of sequence may underlie the TTM/OCD spectrum phenotype (Zuchner et al., 2006). Building on these findings, seven changes in the SAPAP3 were identified in a group of 44 cases who had both TTM and OCD. The changes occurred more frequently in the TTM/OCD group than in the control group, 4.2 % versus 1.1%. It was argued that a combination of these genetic mutations may increase a genetic predisposition to TTM and OCD spectrum disorders but not be directly causal of disease. Further supporting this is that carriers of these mutations were found to meet criteria for a number of other psychological disorders (Zuchner et al., 2009). In addition to the aforementioned genetic contributions, it has also been argued that the serotonin receptor 2A associated gene T102T, and a variant T102C, was more common in those with TTM compared to both healthy controls and those with OCD (Hemmings et al., 2006).

In summary, family studies consistently demonstrate that TTM is more common in first-degree relatives of those with TTM than healthy controls, indicating an element of heritability. Most studies in this area acknowledge that the specific genes identified and level of heritability may create a predisposition to TTM, but research has not yet established causal relationship. Yet, the reviewed literature clearly provides evidence of a biological contribution to the disorder.
1.7 Co-morbidity

Additional diagnoses to TTM were made for 42-50% of individuals in a randomised controlled trial (Diefenbach, Tolin, Hannan, Maltby, & Crocetto, 2006) and 82% of individuals in a phenomenological study (Christenson et al., 1991). However, methodological criticisms have cast doubt on the accuracy of such high estimations of co-morbidity (Elliott & Fuqua, 2000). Co-morbidity differs between men and women. More men have a life time history of OCD, and more women have a life time history of major depressive disorder (MDD) (Christenson, MacKenzie, & Mitchell, 1994). The rate of co-morbidity does not seem to vary with: pulling styles, automatic and focused, nor with those who pull in response to positive or negative emotional cues (Lochner et al., 2010).

One of the most commonly diagnosed comorbid disorders in TTM is MDD with estimates ranging from 10-80%. When professional diagnoses of MDD are self-reported 14% of individuals with TTM experience MDD (Cohen et al., 1995). However, when detected by clinical interview, co-morbid MDD ranged from 2% (Diefenbach et al., 2002) to 49% (Lochner, Seedat, et al., 2005). When individuals with TTM experienced high dissociation, MDD was found in 80% of patients (Diefenbach et al., 2002; Lochner et al., 2004; Streichenwein & Thornby, 1995). Co-morbid anxiety disorders have a prevalence of 15% (Cohen et al., 1995). Generalized anxiety disorder (GAD) was reported as high as 30% in one study (Diefenbach et al., 2002). Other anxiety disorders that appear as comorbid diagnoses include: panic disorder 6%, social anxiety 8-11%, specific phobia or simple phobia 11-18%, and post-traumatic stress disorder 0-5% (Diefenbach et al., 2002; Lochner et al., 2005).

It has been reported that 17% of individuals with TTM use tobacco to relieve negative feelings associated with pulling, 14% use alcohol and 6% use illegal drugs (Woods, Flessner, Franklin, et al., 2006a). These figures are much lower when diagnostic criteria are
applied. For example, alcohol abuse was found to have a 2% life time co-morbidity, alcohol dependence 0%, and substance abuse 4-7% (Cohen et al., 1995; Lochner, Seedat, et al., 2005). In those with TTM, life time co-morbidity of eating disorders were reported as 2% for anorexia nervosa, 6% for bulimia nervosa and 10% for binge eating disorder (Lochner, Seedat, et al., 2005).

A life time co-morbidity of 2% was found for Tourette’s disorder (Lochner, Seedat, et al., 2005) and 5 out of 80 people with TTM had co-morbid tics; 3 females and 2 males. Those with tics touched their face more often than those without. However, no differences in severity or disability were found with the presence tics (Lochner et al., 2010). Other impulse control disorders were relatively uncommon compared to co-morbidity of mood and anxiety disorders: kleptomania life time co-morbidity was estimated at 4%, pyromania 2%, compulsive shopping 4%, hypersexual disorder 0%, and intermittent explosive disorder 6% (Lochner, Seedat, et al., 2005).

Obsessive compulsive personality disorder was equally comorbid as anxiety disorders in terms of life time comorbidity 8-13% (Lochner et al., 2004, 2005). However, only one out of nine patients were diagnosed with borderline personality disorder (Lochner et al., 2004). When individuals with TTM are high in dissociation, 50% meet the criteria for depersonalization disorder (Lochner et al., 2004), that may indicate an overlap with TTM symptoms. Schizotypal personality traits have been found in 1 out of 16 individuals with TTM (Streichenwein & Thornby, 1995). It must be noted that small sample sizes plague the research in this area and further work is needed to better estimate co-morbidity of TTM with personality disorders.
1.8 Phenomenological comparisons between trichotillomania and obsessive compulsive disorder

Repetitive behaviour is a feature of many disorders with which TTM is discussed in the literature; most often it is compared to OCD (e.g. Chamberlain, Fineberg, Blackwell, Robbins, & Sahakian, 2006; Lochner et al., 2004, 2005). Obsessive-compulsive disorder is characterised by the presence of obsessions and/or compulsions. Obsessions are intrusive and recurring thoughts, urges, or images, that are unwanted and typically cause distress. Most individuals with OCD experience both obsessions and compulsions, with compulsive behaviours often aimed at reducing the distress caused by the obsession or the negative consequences of perceived threat (American Psychiatric Association, 2013). Unlike in OCD, individuals with TTM generally do not experience obsessions, nor is hair pulling performed to prevent a dreaded situation from happening (American Psychiatric Association, 2013). Cognitions have been found to play a role in TTM (Rehm et al., 2012), yet the relationship between cognitions and behaviour in TTM is not as clearly defined as it is in OCD.

Compulsions in OCD are defined as repetitive behaviours or mental acts that are performed in response to obsessions and follow rigid rules. Furthermore, they are conducted to reduce the distress associated with the obsession (American Psychiatric Association, 2013). People with TTM experience the repetitive behaviour of pulling out hair, similar to compulsions. However, in contrast to compulsions in OCD, the behaviour of hair pulling does not have a clear and precise psychological definition. The range of cues that activate the behaviour of hair pulling are diverse, numerous and less well defined than repetitive behaviours in OCD (Diefenbach et al., 2002; Mackenzie, Christenson, Lebow, & Mitchell, 1995).

Triggering cues associated with TTM and OCD differ. In OCD cues are typically physically active, and of short duration such as: house cleaning, returning home, leaving
home and getting out of bed. Conversely, tasks which trigger hair pulling are longer in duration and involve minimal physical activity such as: watching television, reading books, doing homework and studying (Mackenzie et al., 1995). Other cues implicated in hair pulling may be: internal, such as positive or negative affective states, cognitions and physical sensations (Du Toit et al., 2001; Mansueto et al., 1999); or external, such as mirrors, tweezers and particular places (Mansueto, Golomb, Thomas, & Sternberger, 1999). Indeed, the hair quality itself may be a cue to pull, such as: coarse, fine, long, short, and dark (Du Toit et al., 2001). OCD differs from TTM in that cues and behaviours in OCD may change over time. For example, washing may be replaced by counting. Generally, this does not happen in TTM. It has been argued that the behaviour in TTM is always hair pulling and is not replaced (Swedo & Leonard, 1992).

Like OCD, a cyclical role of affect has been implicated in TTM, with the experience of tension before pulling and subsequent relief after (Diefenbach et al., 2002; Shusterman, Feld, Baer, & Keuthen, 2009). However, other research supports a more complex role of affect in TTM. Positive, negative, or both, may be experienced before and after pulling (Ferrão et al., 2006; du Toit et al., 2001; Stanley, Swann, Bowers, Davis, & Taylor, 1992; Woods, Flessner, Franklin, et al., 2006a). This broad, and sometimes conflicting, experience of emotion in TTM is in harmony with Macinnis & Patrick's, (2006) model of affect in impulse control. Within this model, an individual may experience a variety of conflicts between complex emotions, depending on whether the impulse is gratified. For example, an individual may experience pride in abstaining from hair pulling and regret for missing out on the pleasure it gives.

Similarly to OCD, emotions experienced during hair pulling behaviour are negative, such as: anxiety, disgust, panic, uneasiness and incompleteness (American Psychiatric Association, 2013). Yet, the wider range of emotions implicated in TTM compared to OCD
seems to reflect both the ego-dystonic nature of hair-pulling, which is not congruent with one’s self perception; and the ego-syntonic nature of hair-pulling, which is congruent with one’s self view. TTM tends to be ego-syntonic during the behaviour of hair pulling, then ego-dystonic afterwards. Conversely, behaviours associated with compulsions in OCD tend to be predominantly ego-dystonic (Ferrão et al., 2006; Vaghi et al., 2018).

The pattern of co-morbidity differs between OCD and TTM. Individuals with TTM tend to have less co-morbid diagnoses. For example, rates of major depressive disorder in TTM have been estimated at 49%, and are 66% in OCD. Further, depressive symptoms are argued to be more severe in OCD (Lochner et al., 2005; Stanley et al., 1992). Accordingly, those with OCD have higher life time disability, more maladaptive beliefs and more likely to have experienced sexual abuse (Lochner, Seedat, et al., 2005). In regards to treatment response, OCD responds to serotonin reuptake inhibitors and cognitive behavioural therapy to a much greater degree than TTM (Lochner, Seedat, et al., 2005).

Hair pulling and skin picking are similar in that individuals who experience associated behaviours, urges and impulses experience them as occurring quickly, reflecting a lack of cognitive involvement and the predominantly motor activity characteristic of impulses (Ferrão et al., 2006). In comparison, as previously discussed, in OCD there is a larger engagement of cognition. As such individuals who experience OCD are able to exercise some delay in their behaviours, reflecting the engagement of time consuming cognitive processes (Ferrão et al., 2006). The most important difference between OCD and TTM in relation to the series of studies contained within this thesis is the differing contributions of impulsivity and compulsivity to the two disorders. In OCD the repetitive behaviours are solely compulsive, motivated by avoidance of punishment. In TTM it is argued that the repetitive behaviours are both compulsive and impulsive; that is, they can be conducted to obtain a reward (Ferrão et al., 2006). While compulsivity in OCD is central to
the disorder, there remains debate and tension in the literature about how, and to what extent impulsive and compulsive behaviour co-exist in TTM. This is explored and discussed in section 1.10.

1.9 Diagnostic classification

In the current DSM 5, TTM is grouped within the Obsessive Compulsive and Related Disorders (OCRD) diagnostic category. This grouping includes disorders which feature the inability to control, inhibit or stop repetitive behaviours (Hollander, Friedberg, Wasserman, Chin-Chin, & Lyengar, 2005; Phillips et al., 2010). Previously, TTM was categorised as an impulse control disorder not otherwise classified. The decision to include TTM in the OCRD diagnostic group remains controversial, even though 71% of experts worldwide agreed to its inclusion. The controversy centres on the partial overlap of validating evidence between TTM and OCD (Phillips et al., 2010) and partial overlap of evidence between TTM and impulse control disorders (Fineberg et al., 2010).

It was recommended that TTM be classified within the OCRD diagnostic category based on differences of treatments and assessments to those used for impulse control disorders (Phillips et al., 2010). However, its classification as an impulse control disorder has been recommended based on similar arguments (Grant, Odlaug, & Potenza, 2007). In fact, it has been suggested that TTM is specifically a motor-impulse control problem (Fineberg et al., 2010). Further uncertainty arises through the continued use of OCD as a comparison group, creating a possible bias in the existing pool of literature in favour of placing TTM with OCRD. Thus, the position of TTM on the impulsivity/compulsivity spectrum is the key aspect driving the discussion of the classification of TTM in the DSM.
1.10 Reward driven impulsivity and punishment driven compulsivity

Both impulsivity and compulsivity have been related to TTM, although the nature of the relationship between the constructs and TTM, and between the constructs themselves, has been a point of debate. Impulsivity has been defined as the tendency to act with less reflection than would those of similar abilities (Dickman, 1990), or as behaving without forethought due to disrupted top-down cognitive control (Dalley, Everitt, & Robbins, 2011). Unlike impulsivity, compulsivity has been described as being persistent, and can occur without relevance to a goal. Compulsiveness has a repetitive halting element known as perseveration, that may limit attentional scope and make extinction of a particular behaviour difficult (Robbins, Curran, & Wit, 2012). It has been argued that attentional control and other higher order cognitive processing have a top down influence on both impulsive and compulsive behaviour, particularly when tasks are attention demanding (Dalley et al., 2011; Dickman, 2000). Descriptions of impulsivity and compulsivity are displayed in figure 1.2, which highlights the overlap between them. The configuration of this overlap has been a focus of tension in the TTM literature.
The motivation underlying impulsive and compulsive behaviour are argued to stem from differing responses to reward and punishment. Impulsive behaviour occurs in response to an immediate acquirable reward, whereas, compulsive behaviour occurs in response to avoidance of punishment (Chamberlain, Fineberg, et al., 2006; Dalley et al., 2011; Ferrão et al., 2006; Fineberg et al., 2010; Flessner, Knopik, & McGearry, 2012; Odlaug, Chamberlain, Schreiber, & Grant, 2013; Robbins et al., 2012; Zuckerman, 1994). For example, as personality traits, a high sensitivity to punishment has been found in those with OCD (Fullana et al., 2004) and high levels of reward-seeking and impulsive behaviours are found in those with bipolar disorder (Bauer et al., 2018). Medications have also demonstrated that reward motivates impulsive behaviour, and punishment motivates compulsive behaviour.
The effects of a serotonin 2C receptor agonist, lorcaserin, was found to reduce motivation to respond impulsively to rewarding stimuli (Higgins, Zeeb, & Fletcher, 2017) and serotonin reuptake inhibitors reduce motivation to perform compulsions (Romanellie, Wu, Gamba, Mojtabai, & Segal, 2014).

The degree of compulsivity and impulsivity involved in a particular disorder can be used to place it on a spectrum of disorders that ranges from impulsivity at one end and compulsivity at the other. For example, OCD at the compulsive extremity, TTM in the middle with combinations of impulsivity and compulsivity, and antisocial personality disorder can be placed at the impulsive end (Hollander et al., 2005; Hollander, 1993). Corresponding to high compulsivity is the experience of overexaggeration of harm, otherwise known as risk aversion, or avoidance of punishment. At the other extreme, associated with impulsiveness, is the underestimation of harm due to a high drive and focus on pleasure, stimulation, and approach to reward (American Psychiatric Association, 2013; Hollander, 1993; Hollander, Friedberg, Wasserman, Yeh, & Iyengar, 2005).
Figure 1.3 A dimensional approach to impulsivity and compulsivity, Hollander et al (2006)

OCD = obsessive compulsive disorder; BDD = body dysmorphic disorder; AN = anorexia nervosa; DEP = depersonalization disorder; HYP = hypochondriasis; TS = Tourette’s syndrome; TTM = trichotillomania; KLEP = kleptomania; PG = pathological gambling; SIB = self-injurious behaviour; SC = sexual compulsions; BPD = borderline personality disorder; ASPD = antisocial personality disorder.

Research on the role of motivation in TTM is yet to produce conclusive results that would assist in appropriately locating it on the impulsive/compulsive spectrum. Specifically, in an attempt to examine the role of reward and punishment as drivers of TTM behaviours Odllaug and colleagues (2013) asked participants with TTM (n=111) whether their pulling was motivated by attempts to relieve anxiety or tension (i.e., avoidance of punishment) or in order to experience pleasure (i.e., reward) (Odllaug et al., 2013). No defining characteristics were found when those with TTM were categorized into one of the two groups. This indicated that the motivation to pull hair is more complex and may entail elements of both types of motivation.
Alternatively, Lochner and colleagues (2005) have challenged the notion of an impulsivity/compulsivity spectrum. Based on comorbidity, clinical variables, cognition, precipitating factors, and treatment response in TTM and OCD a reconceptualization of impulsivity and compulsivity as orthogonal dimensions was suggested (Lochner, Seedat, et al., 2005). That is, individuals are able to have independent levels of impulsivity and compulsivity, and as the level of one changes, the level of the other is not affected. This idea removes TTM from the one dimensional impulsivity/compulsivity spectrum that inadequately captured the complex presentation of the disorder. Further support for the orthogonal relationship was found in a Japanese cohort of individuals with OCD and comorbid impulsive conditions (Matsunaga et al., 2005). Researchers were able to identify differences in demographic and clinical variables between those with and without impulsive conditions. Although, a logistic regression analysis failed to predict the presence of impulsive conditions (Matsunaga et al., 2005). These conflicting findings stimulate discussion in the literature around impulsivity and compulsivity in TTM (Fineberg et al., 2010; Lochner & Stein, 2006; Lochner, Seedat, et al., 2005). While impulsivity and compulsivity can be thought of as distinct categories or continuums, there is some evidence that they overlap. This becomes evident when demographic and clinical variables are assessed using cluster analysis rather than between groups analysis.

Three different clusters were found based on literature exploring OCD related disorders: reward deficiency, impulsivity and somatic concerns. TTM was found to belong to the reward deficiently cluster (Lochner & Stein, 2006). The reward deficiency cluster was associated with early onset age, and presence of tics. Included in this cluster are TTM, pathological gambling, hypersexual disorder and Tourette’s disorder. The name ‘reward deficiency’ was chosen due to altered dopaminergic function in the included disorders. The second cluster, impulsivity, was associated with the female gender and childhood abuse. The
included disorders are: compulsive shopping, kleptomania, eating disorders, self-injury, and intermittent explosive disorder. These disorders all involve an element of impulsivity, hence the name of the cluster. The final cluster, somatic, is associated with low insight, rumination and rituals around appearance and health. It includes body dysmorphic disorder and hypochondriasis (Lochner & Stein, 2006). The inclusion of TTM in the reward deficiency group seems to support the notion that TTM is a compulsively driven disorder rather than an impulsively driven disorder.

Alternatively, others have suggested conceptualisation as an addiction may be more appropriate, in line with TTM’s responsivity to reward (Schreiber, Odlaug, & Grant, 2013). The key characteristics of addiction disorders: repetitive or compulsive engagement in hair-pulling despite adverse consequences; diminished control; an appetitive urge or craving state prior to; and a hedonic quality during hair-pulling; have been found to apply to TTM (Grant & Potenza, 2005). However, this may apply to only a subgroup with TTM. Indeed, a lack of evidence has been cited for not including behavioural addiction disorders with substance addictions, with the exception of gambling and internet addiction (Grant, Potenza, Weinstein, & Gorelick, 2010).

Finally, TTM can be grouped with other body-focused repetitive behaviours (BFRBs) (Phillips et al., 2010) in which the individual directs behaviours towards one’s own body, and typically involves removing parts of the body. This group was originally suggested based on similarities between skin picking and trichotillomania (Bohne, Wilhelm, Keutchen, Baer, & Jenike, 2002); the current diagnostic criteria for excoriation disorder (skin picking) is almost the same as TTM, with only differing behaviours and associated consequences (American Psychiatric Association, 2013). Other BFRBs that could be considered normal grooming behaviours that can occur at clinically significant levels are nail biting, skin biting, skin scratching and chewing on the mouth and lips (Bohne et al.,
Researchers have proposed a model of habit disorders in which to make sense of BFRBs, the ABC model. The model consists of three areas; affect regulation, behavioural addiction, and cognitive control (Stein, Chamberlain, & Fineberg, 2006). Within the ABC model, habit disorders, including TTM, were related to positive reinforcement and reward, similar to those of addiction; by extension relating TTM to impulsivity rather than compulsivity.

The idea that impulsivity and compulsivity can exist on two separate continuums is supported by neuropsychological evidence that points to discrete but intersecting neuroanatomical circuits, figure 1.4. Impulsivity can stem from a ventral striatal loop and a dorsal striatal loop. The ventral striatal loop includes the ventromedial pre frontal cortex, nucleus accumbens and subgenual cingulate cortex. It is associated with delayed discounting, which is a decrease in reward value the longer waiting is required. The dorsal striatal loop includes the ventrolateral prefrontal cortex, anterior cingulate, pre-supplementary motor cortex, caudate and putamen. It is associated with stop signal inhibition, that is, the ability to refrain from responding to a cue, when responding at speed to a different cue. (Robbins et al., 2012; Vaghi et al., 2018). On the other hand, the dorsal and ventral lateral pre-frontal cortex, lateral orbital frontal cortex, and caudate are associated with set shifting and cognitive inflexibility. These are cognitive processes often experienced with behavioural compulsive habits. Compulsive habits are maintained by the avoidance of punishment. It has been argued that the supplementary motor area, premotor cortex and putamen underlie these types of repetitive behaviours (Robbins et al., 2012; Tricomi, Balleine, & Doherty, 2009; Vaghi et al., 2018).

Two types of impulsivity have been proposed, ‘motor impulsivity’ which is behavioural, and ‘reward impulsivity’ in which a person’s behaviour depends on the nature
of the reward. ‘Motor impulsivity’ has been associated with white matter connectivity between the dorsal striatum and the supplementary motor area. ‘Reward impulsivity’ has been associated with white matter connectivity between the ventral striatum and ventromedial dorsolateral prefrontal cortex (Hampton, Alm, Venkatraman, Nugiel, & Olson, 2017). It has been argued that motor impulsivity is the defining feature of TTM (Fineberg et al., 2010), which makes the distinction between motor and reward impulsivity an important one when using neuropsychological findings to make sense of TTM. A type of ‘motor impulsivity’ of interest in TTM is response inhibition, in which individuals try not to respond behaviourally to a stimulus (Chamberlain, Fineberg, et al., 2006; Chamberlain & Sahakian, 2007). The paralimbic cortex has been linked to the function of response inhibition and high impulsivity in healthy individuals (Horn, Dolan, Elliott, Deakin, & Woodruff, 2003). Yet, if TTM was viewed as an addiction, as proposed by Grant et al. (2007) then ‘reward impulsivity’ would be the type of impulsivity of interest.

It could be argued that ‘reward impulsivity’ has important implications for learning the habit of hair pulling in the first place through reinforcement. How accurately a reward can be predicted might influence learning and habit maintenance. The putamen has been found to respond to stimulus-action-dependant reward prediction; that is, the association between a reward and cue, independent of an action by the participant (Haruno & Kawato, 2006). Applied to TTM, this may be similar to the ability to predict whether a pulled hair will result in the required sensation (physical or psychological). Whereas, an error in the prediction of a reward has been found to activate the caudate (Haruno & Kawato, 2006). These findings suggest that different neurological circuits may be associated with reward and punishment responses and may provide a useful method in determining the role of these motivating factors in various psychopathologies as well as assist in identifying common or
distinct neurological underpinning between disorders such as TTM and other OCD spectrum disorders.

Indeed a recent fMRI study supports the notion of both reward and punishment sensitivities, and responses to reward and punishment as important underlying drivers of hair-pulling behaviour (White et al., 2013). This may, in part, explain the difficulties in determining the most suitable classification grouping for TTM in our current diagnostic system. It also highlights the importance of examining the relative contribution or interplay between motivation/drivers and the symptom of the disorder and the need for developing more complex models of development and maintenance of the disorder. There remains considerable debate about diagnostic classification and conceptualization of TTM.

Nevertheless, a range of treatments have been developed to reflect the various aetiological models.
Figure 1.4 Schematic and speculative depiction for four different 'fronto-striatal loops' associated with impulsivity and compulsion; Robbins et al, 2012

Note: vm-PFC: ventromedial prefrontal cortex; SG-Cing: subgenual cingulate cortex; NAc: nucleus accumbens; VS: ventral striatum; vl-PFC ventrolateral prefrontal cortex (including inferior PFC); ACC: anterior cingulate; pre-SMA: pre-supplementary motor area; CAUD: caudate nucleus; PUT: putamen; dl-PFC: dorsolateral prefrontal cortex; dl-PFC: dorsolateral prefrontal cortex; l-OFC: lateral orbitofrontal cortex; SMA: supplementary motor area; PMC: premotor cortex.

1.11 Treatments

Psychological treatments are typically extensions of behaviour therapy, where the behaviour of hair pulling is addressed using traditional learning models (Azrin, Nunn, & Frantz, 1980; Mansueto et al., 1999) and the cognitive and affective experiences associated with the behaviour are targeted with different techniques from multiple approaches (Slikboer, Nedeljkovic, Bowe, & Moulding, 2017). Approximately 10 weekly sessions have been the usual duration for psychological treatment (Flessner, Penzel, & Keuthen, 2010).
Pharmacological treatment approaches target serotonin, norepinephrine, and dopamine systems. Both treatment approaches have been used together resulting in improved outcomes over single modality treatment (Dougherty, Loh, Jenike, & Keuthen, 2006), yet psychological treatments tend to show the most efficacy in randomised trials (Bloch et al., 2007; McGuire et al., 2014; Slikboer, Nedeljkovic, Bowe, & Moulding, 2017), even though, long term relapse rates are as high as 67% (Falkenstein, Rogers, Malloy, & Haaga, 2014). While treatment options are being explored and refined, there is the common perception amongst those receiving treatment that current approaches are inadequate (Woods, Flessner, Franklin, et al., 2006a). For a more detailed review and description of current research on treatment approaches for TTM than what is presented, see Slikboer et al., (2017).

Psychological treatments for TTM began with habit reversal therapy (HRT), a behavioural approach that showed promise, with initial reports showing reduced pulling by 80% (Azrin, Nunn, & Frantz, 1980). The most common elements of HRT used in therapy are: awareness training, competing response training, stimulus control and self-monitoring (Flessner et al., 2010). Another behaviourally based treatment is movement decoupling. It is a self-help treatment that redirects attention away from the behaviour of hair-pulling. It has demonstrated some helpfulness in reducing symptoms (Moritz & Rufer, 2011). Cognitive behaviour therapy (CBT), that added cognitive restructuring, thought stopping and guided self-dialogue to behavioural approaches, is now the most common initial treatment for TTM (Flessner et al., 2010; Lerner, Franklin, Meadows, Hembree, & Foa, 1998). Third wave therapies including acceptance commitment therapy (Woods, Wetterneck, & Flessner, 2006) and dialectical behaviour therapy (Keuthen et al., 2010) have also been added to behaviour therapy and trialled in TTM cohorts, with significant improvements in symptoms.

Evidence supporting serotonergic medications for the treatment of TTM is minimal (Slikboer et al., 2017). Fluoxetine was not found to be useful in reducing TTM symptoms.
(Streichenwein & Thornby, 1995), yet sertraline aids symptom reduction when prescribed with behavioural therapy (Dougherty et al., 2006). Of the tricyclic antidepressants, desipramine and clomipramine, clomipramine was reported to be the more effective treatment (Swedo, Leonard, Rapoport, Lenane, Goldberger, Cheslow, 1989). An atypical antipsychotic olanzapine has also been trialled as a treatment for TTM in which most participants reported symptom improvement (Van Ameringen, Mancini, Patterson, Bennett, & Oakman, 2010). Also demonstrating some improvement in TTM symptoms was the dietary supplement N-acetyl cysteine (Grant, Odlaug, & Kim, 2009).

1.12 Summary

Clinically significant TTM has a prevalence of approximately 1%. However, this is based almost exclusively on student cohorts. It can appear in childhood, adolescence or adulthood and is typically chronic, although when onset occurs in childhood it may remit at puberty. Hair can be pulled from any part of the body, with the most common being from the scalp and eyes. The only styles of hair pulling to consistently appear in the literature are that of automatic and focused pulling, yet recent work has challenged their definition. An element of heritability has been implicated with higher than random occurrences of TTM in family members than in controls. Co-morbidity is common, with depressive and anxiety disorders most common, followed by OCD and impulse control disorders. Both psychological and pharmacological treatments are available and many have shown promise, yet our lack of understanding about what motivates hair-pulling behaviour maybe hampering efforts to improve treatment outcomes.

Classifying TTM has been challenging due to symptom overlap with other disorders and other diagnostic categories. Much of the literature explores this problem by comparing
heritability, comorbidity, phenomenology, underlying brain structures, neuropsychology, and treatment efficacy to OCD. The current placement of TTM with the obsessive compulsive and related disorders diagnostic group is based on this evidence. Only a small number of studies attempt to explore reward and punishment in TTM, and those that do tend to use designs or measures that are somewhat removed from the actual variables. Further, in recent research, TTM is more frequently compared to OCD, rather than to impulse control disorders or addiction. This may have led to the false impression that TTM is more closely associated with compulsiveness than is warranted. Impulsive and compulsive behaviours are defined by the influence of reward and punishment; directly quantifying their strength in TTM is vital for understanding the motivation underlying the behaviour of hair pulling.
2 Models and conceptualizations of trichotillomania
The ambiguity in the reviewed literature regarding prevalence, pulling styles and sub-types, co-morbidity, and nosology, points to an incomplete, unclear and/or unstable idea of how we understand, make sense of, and define TTM. Prior to designing a research program in which the main objective is to improve our understanding of TTM, it is necessary to establish a starting point; that is, summarise how do we already make sense of, and understand, TTM. Much of the information presented in chapter one was descriptive or theoretical. In chapter two, a more critical and focused approach is taken to exploring existing models of TTM. As the objective is to address our understanding of TTM, only models that exclusively and explicitly proposed a defined structure that attempts to explain TTM were included. This excludes models attempting to characterise TTM within larger groups of disorders.

2.1 Comprehensive Behavioural Model

Currently, the lead psychological model for understanding TTM is the comprehensive behavioural model (CBM; Mansueto et al., 1999). The CBM is based on the traditional learning theories of classical and operant conditioning. It takes into account a wide range of phenomena associated with TTM, and categorises these phenomenon into four distinct groups: conditioned stimuli/cues, discriminative stimuli, behaviours, and consequences (Mansueto, Stemberger, Thomas, & Golomb, 1997). The CBM is versatile; that is, almost any stimulus can be allocated into any of the four groups.
Table 2.1 Summary of Components of the Comprehensive Behavioural Model

<table>
<thead>
<tr>
<th>Components</th>
<th>Examples</th>
</tr>
</thead>
<tbody>
<tr>
<td>I. Conditioned stimuli/cues</td>
<td></td>
</tr>
<tr>
<td>External</td>
<td>Bathroom, car</td>
</tr>
<tr>
<td>• Settings</td>
<td>Tweezers, mirror</td>
</tr>
<tr>
<td>Internal</td>
<td></td>
</tr>
<tr>
<td>• Affective states</td>
<td>Anxiety, boredom</td>
</tr>
<tr>
<td>• Sensations</td>
<td>White hair, coarse hair</td>
</tr>
<tr>
<td>• Cognitions</td>
<td>“My hair must be even”</td>
</tr>
<tr>
<td>II. Discriminative stimuli</td>
<td></td>
</tr>
<tr>
<td>External</td>
<td></td>
</tr>
<tr>
<td>• Absence of others</td>
<td></td>
</tr>
<tr>
<td>• Presence of implements</td>
<td></td>
</tr>
<tr>
<td>Internal</td>
<td></td>
</tr>
<tr>
<td>• Urge/impulse</td>
<td>Hand near scalp, unoccupied</td>
</tr>
<tr>
<td>• Posture</td>
<td>“I’ll only pull one” “someone might walk in”</td>
</tr>
<tr>
<td>• Cognition</td>
<td></td>
</tr>
<tr>
<td>III. Behaviours</td>
<td></td>
</tr>
<tr>
<td>Preparatory</td>
<td>Go to private place, visual/tactile search</td>
</tr>
<tr>
<td>Pulling</td>
<td>Right, left, both hands; twist, twirl; root/no root; single hair/tufts</td>
</tr>
<tr>
<td>Disposition</td>
<td>Eating; saving; discarding</td>
</tr>
<tr>
<td>IV. Consequences</td>
<td></td>
</tr>
<tr>
<td>Reinforcing</td>
<td>Increase/decrease sensation; distraction; obtaining hair/root; obtain goal (e.g. symmetry)</td>
</tr>
<tr>
<td>Aversive</td>
<td>Negative emotional states; negative sensations (pain)</td>
</tr>
</tbody>
</table>

Note: Mansueto et al., (1997)

The CBM explains how an urge to pull hair develops. Firstly, a pattern of behaviour develops, through classical learning, and an urge to pull becomes associated with this pattern. The urge then triggers more pulling behaviour in response to a continually increasing variety of cues (Mackenzie et al., 1995; Mansueto et al., 1997). This explanation for the behaviour of pulling is circular; the behavioural pattern already needs to be in place before more hair pulling behaviour occurs, making this a model of maintaining factors. The model was proposed as a guide for clinicians, to help them conceptualize treatment; and for researchers, to aid the generation of hypotheses (Mansueto et al., 1997). Most psychological treatments for TTM have a behavioural component based on this model in the form of HRT. HRT is the most evidence-based treatment for TTM.
As noted by Mouton and Stanley (1996), viewing TTM as purely behavioural does not address how the cycle of hair-pulling behaviour begins or what is the underlying motivation or drive behind hair pulling. Within the model, reinforcing and aversive stimuli are described and situated as a consequence of pulling out hair (Mansueto et al., 1997), not as the driving stimuli behind hair pulling behaviour. Therefore, HRT was built on the idea of reinforcing and aversive outcomes that occur after and in response to hair that has already been pulled out. The consequence of this is that treatments based on HRT addresses the symptoms of TTM, but not the underlying cause. This has been reflected in the lack of evidence demonstrating long term efficacy for HRT alone and the predominance of short term symptom reduction (Slikboer et al., 2017).

2.2 Biopsychosocial Model

The CBM of TTM has been extended to include biological vulnerability to the mix of classic learning mechanisms (Franklin, Tolin, & Diefenbach, 2006). It is theorised that a biological vulnerability predisposes one to altered pain sensitivity and negative internal states, figure 2.1. In turn, the altered pain sensitivity and internal states contribute to maintaining symptoms. The value of the Biopsychosocial model is heuristic; that is, generating ideas for research and for clinicians. There is some support for the individual elements included in the model but there is a lack of empirical support for the overall model.
The element ‘biological vulnerability’ has been demonstrated in a family study (Keuthen et al., 2014), and ‘negative social’ consequences of disclosing TTM have been identified (Marcks, Woods, & Ridosko, 2005). Although, recent research has cast doubt on the role of pain sensitivity in TTM (Blum, Redden, & Grant, 2017), this sensory aspect of TTM may be better described as sensory over-responsivity (Falkenstein, Conelea, Garner, & Haaga, 2018). Within the model ‘increased pleasurable sensations’ are proposed as part of TTM, based on a small study (Stanley et al., 1992) in which those with TTM are compared to those with OCD. This is problematic because the results do not tell us if those with TTM experience more pleasure than healthy controls, only that they experience more pleasure.
than those with OCD. Indeed, the diagnostic criteria ‘experienced pleasure, gratification, or relief after pulling’ has been removed from the DSM due to a lack of supporting evidence (American Psychiatric Association, 2013; Lochner et al., 2012).

Like the CBM, the biopsychosocial model seems to explain how symptoms continue. It does not address specific underlying motivations or drives and psychological processes. The model is not specific about what constitutes many of the individual elements; for example, it is left up to the reader to decide what the ‘negative social and emotional consequences’ are, making the model incomplete. Much of the supporting evidence presented for ‘altered pain sensitivity’ and ‘biological vulnerability’ (Franklin et al., 2006) is inconclusive. While the direction of the arrows within the model make sense intuitively, empirical evidence for their direction is needed.

2.3 The ethological model of trichotillomania

Ethology is the study of animal behaviours within and between species; it includes the application of purpose and meanings to these behaviours. A type of behaviour called a ‘fixed-action pattern’ is the key feature of the ethological model of TTM (Swedo & Rapoport, 1991; Swedo, 1989; Susan Swedo & Leonard, 1992). Examples of fixed-action patterns are the pecking and scratching of a new hatchlings, and dogs turning in circles to trample grass before lying down, regardless where it sleeps (Swedo, 1989). A fixed-action pattern is an internally generated pre-programed sequence of behaviour released by a specific external stimulus that is performed to completion (Moltz, 1965). The internal generation of the fixed-action pattern is evident, as the behaviour is only delayed, not absent, when the releasing stimulus is withheld. They are rigidly stereotyped; and they actualize without learning or modelling. A behaviour that continues the fixed-action pattern has been
termed an orientating movement or a taxi. (Moltz, 1965). The combination of a taxi and fixed-action pattern result in the observable behaviour. See figure 2.2 for a visual representation of a fixed-action pattern.

Figure 2.2 An ethological model of behaviour; Swedo (1989).

It has been argued that the ethological model of TTM is an attempt to explain the origin of hair-pulling behaviour, as opposed to how the behaviour is maintained (Mouton & Stanley, 1996; Susan Swedo & Leonard, 1992). The model is often referred to in more
recent reviews of TTM (Chamberlain, Odlaug, Boulougouris, Fineberg, & Grant, 2009; Diefenbach et al., 2000; Duke et al., 2010; Penzel, 2003; Teng et al., 2002) indicating it holds some usefulness when trying to make sense of TTM. Evidence supporting the validity of the model has been presented in mice (Garner, Weisker, Dufour, & Mench, 2004), and birds (Bordnick, Thyer, & Ritchie, 1994). However, underlying biological contributions to barbering in mice and feather plucking in birds remains unclear and multifaceted. The model has not been translated into treatments for TTM, but has been argued to influence the creation of the Stimulus Regulation model.

### 2.4 Stimulus Regulation Model

Another model taking into account biological contributions to TTM is the stimulus regulation model (Penzel, 2003, 2008) see figure 2.3. The stimulus regulation model is based on the premise that hair pulling is carried out to maintain arousal levels and homeostasis by stimulating nerve endings in the skin: a type of ‘sensory balance’. This is argued to be the cause of hair-pulling behaviour within the model. It is proposed that an individual has a genetic predisposition for abnormal levels of serotonin and dopamine, which ultimately leads to under or overstimulation. When an individual is over stimulated or under stimulated they pull hair to bring themselves back into balance (Penzel, 2003, 2008). It is argued that the stimulus regulation model is an integrated theory, in which the comprehensive behavioural model, the ethological model and neurobiological models are incorporated. This model is based on clinical experience with no research or testing of the theory carried out.
2.5 Limitations of existing models

No *a priori* studies have been identified that aim to test or refine a model. Such a study, for example, could test the stimulus regulation model. It would be expected that in a cohort of people with hair-pulling symptoms, the further measures of arousal are from the mean of a healthy control group, the more severe the symptoms of hair-pulling behaviour. Another example is that if the biopsychosocial model holds true, then structural equation modelling would be able to demonstrate the stability of a feedback loop (non-recursive model) between hair-pulling behaviour and hair-pulling urges (Fox, 1980). In addition, biological vulnerability, negative internal states, and discriminative cues would be independent latent variables with a relationship to either urges or pulling behaviour. Such studies being explicitly deducted from the reviewed models have not been identified. Rather the models presented have been proposed *a posteriori*; that is, they were developed from existing knowledge. Confirmatory studies of the reviewed models are needed to develop, update and increase confidence in them.

*Figure 2.3 How pulling regulates internal levels of stimulation; Penzel (2003)*
The CBM, biopsychosocial and stimulus regulation models are versatile but in some ways lack specificity. The stimulus regulation model implicates dopamine and serotonin. However, results of randomised controlled trials of serotonin reuptake inhibitors, which have secondary properties effecting dopamine, suggest only a very small decrease in hair pulling symptoms (Christenson, Mackenzie, Mitchell, & Callies, 1991; Streichenwein & Thornby, 1995; van Minnen, Hoogduin, Keijsers, Hellenbrand, & Hendriks, 2003), casting doubt on the stimulus regulation model. When serotonin based medications are used to treat TTM the reduction of symptoms is so minor that the clinical usefulness of serotonin reuptake inhibitors in reducing hair pulling behaviour is questionable. Accordingly, researchers are investigating other medications that primarily target dopamine (Van Ameringen, Mancini, Patterson, Bennett, & Oakman, 2010), and the glutamate system (Grant et al., 2009).

The CBM and the biopsychological model rely heavily on learning theories. However, research has only been able to explain a small range of emotional patterns related to hair pulling in terms of learning theory (Diefenbach et al., 2002). Further, the role of cognitions in TTM has only recently been explored (Rehm, et al., 2012). In fact, most of the literature explores phenomenology and efficacy of treatment; only a few directly aim to develop a psychological model based on statistical evidence (Flessner, Woods, Franklin, Cashin, & Keuthen, 2007; Norberg, Wetterneck, Woods, & Conelea, 2007). The CBM and biopsychosocial models do not examine the key drives that motivate hair-pulling behaviour. These two models are perhaps the most relevant to current treatment, which is predominantly CBT (Flessner et al., 2010). Indeed, the lack of meta-analytical evidence supporting long-term reduction in TTM symptoms (Bate, Malouff, Thorsteinsson, & Bhullar, 2011; McGuire et al., 2014; Slikboer, Reser, Nedeljkovic, Castle, & Rossell, 2017)
may reflect the absence of key drivers and motivation in the CBM and biopsychosocial models.

Further, some psychological therapies for TTM seem to have been developed irrespective of the TTM models, widening the gap in the literature between existing psychological models of TTM and outcome studies (Slikboer et al., 2017; Slikboer, 2013). For example, ACT (Woods, Wetterneck, & Flessner, 2006) includes six main elements: being present, cognitive diffusion, acceptance, self-as-context, values, and committed action, and was developed on the theory that language and cognition are developed in context (Harris, 2009; Hayes, Luoma, Bond, Masuda, & Lillis, 2006). These elements do not appear in the most recent models of TTM, these being the stimulus regulation model and biopsychosocial model (Franklin et al., 2006; Penzel, 2008). The lack of treatment process and change process studies in TTM may exacerbate this problem. In OCD, process studies have elucidated mechanisms of change within models of OCD and types of treatment (Polman, Bouman, Hout, Jong, & Boer, 2010). Linking models of treatment and models of TTM together in this way would be an invaluable source of information for clinicians.

Biological contributions to TTM and underlying personality factors lack integration into the reviewed models of TTM. The inclusion of biological factors within the models are superficial or unclear irrespective of neuroimaging research being published as early as 1991 (Swedo et al., 1991). More recently, a number of neurobiological hypotheses have been put forward which have not been integrated into a cohesive biological understanding or model of TTM. For example, that of frontal-striatal circuitry (Roos, Grant, Fouche, Stein, & Lochner, 2015), excess of cortical thickness (Odlaug, Chamberlain, Derbyshire, Leppink, & Grant, 2014), and dysfunctional reward processing of the nucleus accumbens (White et al., 2013). The influence of personality even as a predisposition to TTM, has not been included in any models. Yet personality research in a non-clinical sample of hair-pullers was
published in 1994. It demonstrated high trait neuroticism in those with sub-clinical hair-pulling (Stanley et al., 1994) and has recently been found to be predictive of clinical level TTM (Keuthen, Tung, Altenburger, et al., 2015).

Existing models do not explicitly include the role of personality, or trait characteristics e.g., impulsivity, compulsivity and neuroticism as a predisposing factor for TTM. Given the considerable debate in the literature around the contributions of reward and punishment, and the implicit reliance of reward and punishment in the TTM models reviewed, the role of personality could be considered central in how reward and punishment are experienced. A deeper and more integrated understanding of impulsive behaviour driven by reward seeking, and compulsive behaviour driven by avoidance of punishment would be invaluable to future treatment developments and our understanding of what drives hair-pulling behaviour.
3 The Reinforcement Sensitivity Theory of Personality
3.1 What is the Reinforcement Sensitivity Theory of Personality?

In traditional animal behavioural models, variables that influence behaviour are desire and aversion, conceptualised on a single continuum with aversive at one end and desirable at the other (Beck, 2004). More recently, desire and aversion have been reconceptualised in humans as sensitivity to punishment and sensitivity to reward (Carver & White, 1994). Both of these co-exist within an individual on separate continuums ranging from low to high sensitivity. According to RST individuals experience differing levels of reward and punishment based on biological processes, that underlie personality, behaviour and by extension psychopathology (Corr, 2004).

Sensitivity to reward and punishment are key elements of personality. Within the reinforcement sensitivity theory of personality, they underlie certain categories of behaviour and emotional experience (RST; Corr, 2004; Gray & McNaughton, 2000; Smillie, 2008). The origins of RST came from neurobiological evidence from animal experiments (Gray & McNaughton, 2000; Gray, 1987, 1990) and it has successfully been applied and tested in humans (Alimoradi, 2011; Aubi & Alimoradi, 2011; Blanchard, Hynd, Minke, Minemoto, & Blanchard, 2001; Coombes, Naugle, Barnes, Cauraugh, & Janelle, 2011; Perkins, Inchley-Mort, Pickering, Corr, & Burgess, 2012; Smillie, Dalgleish, & Jackson, 2007). A recent update of the RST has resulted in the inclusion of three systems and is now referred to as the revised reinforcement sensitivity theory (r-RST) (Corr & McNaughton, 2008).

These three systems are: the behavioural inhibition system (BIS), in which anxiety is said to help resolve conflict; the behavioural activation system (BAS), associated with feelings of hope and anticipatory pleasure leading to impulsiveness; and the fight/flight/freeze system (FFFS), associated with the emotion of fear leading to avoidance (Table 3.1).
Table 3.1 Emotions/states and Behaviours Associated with the Avoidance of (FFFS) and Approach (BIS) to Aversive Stimuli, and the Approach to Appetitive Stimuli

<table>
<thead>
<tr>
<th>Stimulus conditions</th>
<th>Emotion/State</th>
<th>Behaviours</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Aversive stimuli</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Avoid (FFFS):</td>
<td>Avoidable</td>
<td>Fear</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Phobic avoidance, Escape, Flight</td>
</tr>
<tr>
<td></td>
<td>Unavoidable</td>
<td>Panic</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Fight (defensive aggression), Freeze</td>
</tr>
<tr>
<td>Approach (BIS):</td>
<td>Avoidable</td>
<td>Anxiety</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Behavioural inhibition, Risk assessment</td>
</tr>
<tr>
<td></td>
<td>Unavoidable</td>
<td>Depression</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Behavioural suppression</td>
</tr>
<tr>
<td><strong>Appetitive stimuli</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Approach (BAS)</td>
<td>Attainable</td>
<td>Hope, Anticipatory pleasure</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Exploration, Sub-goal scaffolding</td>
</tr>
<tr>
<td></td>
<td>Unattainable</td>
<td>Frustration, Anger</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Fight (predatory aggression), Displacement activity</td>
</tr>
</tbody>
</table>

Note: Corr (2008)

Activation of the BIS and FFFS can be measured by an individual’s sensitivity to punishment. Likewise, the BAS can be measured by an individual’s sensitivity to reward (Torrubia, Avila, Molto, & Caseras, 2001). More recently the concept of constraint, a system that exerts executive control over the BIS, BAS, and FFFS has been added to r-RST (Kennis, Rademaker, & Geuze, 2013). The four behavioural systems integrate research across multiple levels of inquiry; emotional, behavioural, cognitive, personality, and biological. The behavioural systems stem from their own underlying neurological networks, presented in figure 3.1 below.
Figure 3.1 Overview of the neurobiological systems underlying individual differences in behaviour; Kennis et al, 2013

Abbreviations: FFFS = fight, flight, freeze system, BAS = behavioural approach system, BIS = behavioral inhibition system, PFC = prefrontal cortex, ACC = anterior cingulate cortex, mHypothalamus = medial hypothalamus, PAG = periaqueductal grey, PCC = posterior cingulate cortex, SHS = septohippocampal system, and VTA = ventral
These specific neuroanatomical regions and circuits have been proposed as the location of defined categories of behaviour; i.e., defensive avoidance (FFFS), defensive approach (BIS) and approach (BAS) behaviours (Corr & McNaughton, 2008). Within the r-RST abnormal function of the septo-hippocampal system contributes to anxiety (Gray & McNaughton, 2000). A further notion inherent in r-RST is that rapid behaviour in response to stimuli that elicit fear and anxiety must be mediated by neurobiological systems involved in involuntary processing. These systems include areas such as the amygdala, hypothalamus, and septo-hippocampal system that become hyper-reactive in disorders such as OCD and GAD (Corr, 2008). Some parallels can be drawn between this description of r-RST and knowledge of TTM. Examples are; abnormalities of the amygdala (Isobe et al., 2018), a tendency for those with TTM to experience high anxiety (Keuthen, Tung, Altenburger, et al., 2015; Neal-Barnett et al., 2011), and hair-pulling behaviour described as being rapid and involuntary (Rehm, Nedeljkovic, Thomas, & Moulding, 2015).

The intensity and type of behaviour that occurs in response to threat depends on two important ethological observations: defensive direction and defensive distance (Corr, 2008). Defensive direction is the choice of whether to approach a threat, which engages the BIS, or to avoid a threat, which engages the FFFS (figure 3.2). Defensive distance is how far away the threat is; the intensity of approach or avoidance behaviours depends on the defensive distance. The distance can be measured as actual distance between threat and organism (Blanchard & Blanchard, 1989), or the distance can be psychological. In animals, the distance between prey and predator may be small, which leads to defensive attack behaviour. In humans a small defensive distance may be the belief that one is about to die in the absence of threatening stimuli (McNaughton & Corr, 2004).
Figure 3.2 The relationship between defensive distance, behaviour and possibility of escape; Blanchard and Blanchard (1989)

<table>
<thead>
<tr>
<th>System state</th>
<th>Defensive distance</th>
<th>Real distance sufficient to elicit reaction</th>
</tr>
</thead>
<tbody>
<tr>
<td>Low defensive individual</td>
<td>Perceived distance &gt; actual distance</td>
<td>Short</td>
</tr>
<tr>
<td>Normal defensive individual</td>
<td>Perceived distance = actual distance</td>
<td>Medium</td>
</tr>
<tr>
<td>High defensive individual</td>
<td>Perceived distance &lt; actual distance</td>
<td>Long</td>
</tr>
</tbody>
</table>

Note: from Corr, (2008), pg. 15.
The defensive distance becomes larger if an organism is particularly brave or if the threat is not perceived to be very salient. The defensive distance becomes smaller if the organism is prone to fear or if the threat is perceived as very salient (Corr, 2008). In TTM a very salient threat of short distance might be the immediate public disclosure of baldness due to hair-pulling; if the individual is highly sensitive to punishment the defensive distance will seem shorter than what it could be. As defensive distance underlies behavioural reaction to threat, and all behaviour is mediated by neural regions in r-RST, it follows that the underlying neural networks of defensive approach and defensive avoidance, are organised according to defensive distance, figure 3.4. The periaqueductal grey, medial hypothalamus and ventral medial hypothalamus, are associated with the smallest defensive distances (McNaughton & Corr, 2008).

![Figure 3.3 The two-dimensional defence system; McNaughton & Corr (2004)](image-url)
The most useful aspect of r-RST for the current research is that r-RST brings together two different areas of research; personality (i.e., behaviour, emotion, motivation and cognition), and neuroscience, both structural and functional (Collins, Jackson, Walker, Connor, & Gardiner, 2017; Corr & McNaughton, 2008; Smillie, 2008). It is able to explain personality within an individual, between individuals, and between groups (Collins et al., 2017).

3.2 The behavioural inhibition system

Learning and motivation have been found to contribute to approach and avoidance behaviours within r-RST in humans (Smillie et al., 2007). Awareness of this relationship goes back to Miller’s theory of conflict, which was based on animal experiments (Miller, 1971). Miller found that, in the case of reward, the closer an organism is to a stimulus the more motivated the organism is to reach it. Likewise, with avoidance, the closer the organism is to the stimulus the more motivated the organism is to avoid it. The underlying motivation to approach or avoid a stimulus can be strengthened through learning; i.e., when an organism is repeatedly exposed to the stimulus (Miller, 1971). When Miller paired food with electric shock, the observed behaviour of a mouse was to vacillate between approach and avoidance (Beck, 2004). This behaviour is similar to those resulting from the BIS. The BIS inhibits avoidance behaviours so that the organism is able to explore and conduct risk assessment. Within the BIS, such behaviour does not only occur in response to approach-avoidance conflict, but also with approach-approach; and avoidance-avoidance conflicts (Corr, 2008).

When faced with an approach-approach conflict, i.e., wanting to approach two different goals at the same time, as the organism moves towards the first goal, the
motivation to approach the goal becomes stronger. Therefore, the motivation to approach the second goal is weakened, so the conflict is easily avoided. When faced with an avoidance-avoidance conflict and escape is not possible, the organism finds the point of least distress between the two. In an avoidance-avoidance conflict, the organism moves away from one, but in doing so, it moves towards the other. The point of least distress is in the middle where the organism remains immobile. If the organism cannot escape the situation physically, it will psychologically. In this case, motivation is focused on psychological escape by forgetting, sleeping or drugs (Corr, 2008).

Activation of the BIS is caused by conflicting emotions and/or goals; this is illustrated in figure 3.3 where the BAS and FFFS feed forward into the BIS. For example, the desire to approach the bathroom in which hair pulling is carried out (BAS stimulus) conflicting with the need to avoid hurtful comments from a family member who happens to be in the bathroom (FFFS stimulus). Indeed, humans are able to make predictions about their own affective states, called affective forecasting (Macinnis & Patrick, 2006). Therefore, conflicts may exist in a perceived future, which in turn influences decision making and behaviour in the present (Macinnis & Patrick, 2006). Extending the current example, the conflict between approaching the bathroom and avoiding the family member can be imagined to occur in the future, resulting in ambivalence and anxiety about carrying out the behaviour of hair pulling in the first place.
Within the BIS, the anxiety from such conflicts has the function to bring the organism closer to the threat; this is called defensive approach (McNaughton & Corr, 2004; Pickering & Corr, 2002). Again using our example to illustrate BIS behaviour, this means that one would slowly approach the bathroom while watching the family member to make sure it is safe. In animal models the threat is a predator. In humans the threat only needs to be a perceived, such as a belief, a thought, a story or an image (Blanchard et al., 2001; Coombes et al., 2011).

The BIS aims to resolve goal conflict via a negative feedback loop between threat stimuli from the FFFS and its negative valence. Behaviours associated with this process are: risk assessment, scanning of the environment, and scanning of memory. Individuals experience this state as worry and rumination. In terms of personality, the BIS is

Figure 3.4 Biobehavioural architecture comprising reinforcement sensitivity as understood from the perspective of RST; Smillie (2008).
experienced as worry-proneness and anxious rumination, thereby maintaining an attitude of alertness for danger. A highly activated BIS may result in generalized anxiety and obsessive compulsive disorder; if the BIS is not activated enough the individual may take unnecessary dangerous risks (Corr, 2004; Corr, 2008).

In the BIS, when defensive distance is almost nil, there is a lack of behaviour, inactivity and motionlessness, although with a different quality and posture to that of freezing. At moderate distances risk assessment behaviours become apparent. At long distances normal behaviour occurs (Blanchard & Blanchard, 1989). In table 3.1, pg. 45, emotions and behaviours differ in response to whether the threat is avoidable or not. If avoidable, anxiety, risk assessment and behaviour inhibition occur; if the threat is unavoidable, depression and behavioural suppression occurs (Corr & McNaughton, 2008).

3.3 The fight, flight and freeze system

The FFFS, and associated behaviours, are based on defensive distance and whether escaping the situation is possible (McNaughton & Corr, 2004; Figure 3.3). At very small defensive distances attack behaviour occurs, at medium distances flight or freeze behaviours occur. At large distances there is non-defensive behaviour (McNaughton & Corr, 2004). Behaviours resulting from the FFFS are avoidance and escape, the purpose of which is to bring the organism to safety. Individuals experience this state as fear; in terms of personality it is experienced as fear-proneness and avoidance. Disorders such as panic and phobias reflect an over active FFFS (Corr, 2008).

Separate neuronal networks in the brain give rise to specific behaviours of freezing, fighting or fleeing of the FFFS. These neuronal networks also give rise to emotions such as panic and cognitions. These separate behaviours are all elicited by predatory threat for which
organisms have evolved a coordinating neuronal network system. The purpose of this is to select behaviour in response to threat (Corr, 2008). In humans, an over reliance on one of these neuronal networks may increase the behavioural response to a point where therapy is required. Figure 3.4, pg. 52 displays how psychopathology, defensive distance, defensive approach and defensive avoidance may be associated with specific brain regions within the neuro-behavioural hierarchies. Brain regions are allocated to levels on the defensive avoidance and defensive approach hierarchies based on response to anti-anxiety medications and defensive distance (RST; Corr, 2004; Gray & McNaughton, 2000; Smillie, 2008).

3.4 The behavioural activation system

The third behavioural system in the r-RST is the BAS. Approach behaviours result from BAS activation in response to rewards. In both the r-RST and behaviour theories, reward was defined as “events that increase the probability of future emission of responses upon which they are made contingent” (Gray, 1987). This definition of reward also includes the removal of punishing stimuli. The role or purpose of the BAS is to move the organism closer in time and space to the final biological reinforcer (Corr, 2004). In r-RST terminology, stimuli associated with the drive to move from a state of anticipation to the final biological reinforcer, are termed appetitive stimuli (Corr, 2004). According to r-RST, the drive to attain the biological reinforcer, and the approach behaviour to acquire it, is associated with the state of hope. When expanded to a personality trait this system gives rise to optimism, reward-orientation and impulsiveness (Corr, 2004). Like all the behavioural systems of the r-RST, the BAS personality trait is underpinned by a specific neural net work, presented in figure 3.5.
Impulsiveness within the BAS includes the role of planning in the acquisition of biological reinforcers or the appetitive stimuli. The drive or incentive to reach the biological reinforcer is independent and distinct from the consummatory act (Corr, 2008; Gard, Gard, Kring, & John, 2006). The consummatory act of the biological reinforcer is the end point of a complex process involving many elements, including the role of cognition in planning. The approach behaviour may require the use of sub-goal scaffolding, forethought, behaviour restraint, and problem solving to get closer to the biological reinforcer. However, once reached, impulsivity is needed in the consummatory act. Without contributions of planning
within the BAS one would be left with only immediate impulsiveness. Impulsiveness without planning may increase the time and distance away from the biological reinforcer. Without the resultant behavioural restraint of planning, the organism responds to only immediately accessible appetitive stimuli. Behavioural restraint is the role of the BIS. The BAS is not solely responsible for approach behaviours, as it does not operate in isolation. An underactive BIS or an over active BAS may result in impulsiveness at inappropriate times (Corr, 2008). Other behaviours associated with the BAS may occur that do not actually achieve this goal; they are known as displacement behaviours (Corr & McNaughton, 2008). Grooming behaviours in animals have been thought of as displacement activities (Tinbergen, 1952).

3.5 Constraint

The BIS, BAS and FFFS, having been derived from animal models has been criticised for ignoring the ability of humans to cognitively process information, and respond behaviourally to those cognitions. Further, the BIS, BAS and FFFS does not address how cognition and meta-cognition mediates/moderates behaviour arising from underlying neural networks and emotion (Matthews, 2008). By extension, the various levels of conscious control humans have over behaviour remains unaccounted for (Corr, 2008). r-RST provides an adequate framework in which to explore motivation in TTM, but is an incomplete theory on which to explore a psychological disorder without the inclusion of constraint. Constraint was proposed as an additional and separate personality trait to the BIS, BAS and FFFS (Carver, 2005). Constraint refers to a broad set of prefrontal processes including: effortful control, the use of higher executive functions, volition, and deliberate top-down control over
behaviour and cognition. Constraint can exert regulatory control over the other systems by overriding the impulse to act or desire not to act (Kennis et al., 2013).

r-RST integrates the levels of enquiry of biological (brain regions and arousal), trait (personality), behavioural (approach/avoidance), and psychological (constraint). Higher order cognitive processes that characterise constraint arise from the prefrontal cortex and anterior cingulate cortex. Constraint can override the three behavioural systems FFFS, BIS and BAS and their associated neuropsychological networks (Kennis et al., 2013).

3.6 Magnetic resonance imaging and underlying neural networks of the reinforcement sensitivity theory of personality

The specific types of ‘reward’ in neuroscience – liking and wanting – based on their associated neural pathways (Smith, Tindell, Aldridge, & Berridge, 2009) along with their equivalent on the level of personality, may go some way in explaining the ambivalence around hair-pulling behaviour (Rehm et al., 2015). A number of overlapping concepts have been identified between personality research (usually operationalised with self report questionnaires) and neuroscience (using imaging technology). Similarities between the BAS and the neuroscience ‘reward’ exemplify this, presented in table 3.3 below (Krupić & Corr, 2017). For example, the use of questionnaires and positron emission tomography revealed that underlying individual differences in BAS and reward seeking behaviour could be explained by the availability of opioid receptors in the frontal cortex, amygdala, ventral striatum, brain stem, cingulate cortex, and insula (Karjalainen et al., 2018). In the table below it can be seen that opiates underlie ‘Liking’, the hedonistic pleasure of an experience (Berridge, Robinson, & Aldridge, 2009; Krupić & Corr, 2017).
**Table 3.3 Summary of the BAS Processes and Terminology Clarification**

<table>
<thead>
<tr>
<th>BAS process</th>
<th>Scales</th>
<th>Description</th>
<th>Dominant neurotransmitter</th>
<th>Big five correlates</th>
</tr>
</thead>
<tbody>
<tr>
<td>Wanting (capturing)</td>
<td>SR, Impulsivity and Fun Seeking*</td>
<td>Desire to possess resources</td>
<td>Testosterone</td>
<td>Extraversion, Agreeableness (-) and Conscientiousness (-)</td>
</tr>
<tr>
<td>Incentive motivation (wanting)</td>
<td>BAS-RSQ, BAS-J5 and Reward Interest</td>
<td>Identification and seeking new resources</td>
<td>Dopamine</td>
<td>Openness and Extraversion</td>
</tr>
<tr>
<td>Striving (striving)</td>
<td>Drive and Goal/Drive Persistence</td>
<td>Investing effort in goal-achievement</td>
<td>Serotonin</td>
<td>Conscientiousness and Extraversion</td>
</tr>
<tr>
<td>Liking (liking)</td>
<td>Reward Responsiveness and Reward Reactivity</td>
<td>Reactions to receiving a reward</td>
<td>Endogenous opiates</td>
<td>Extraversion and Agreeableness</td>
</tr>
</tbody>
</table>


To ease comprehension of the relabelling of descriptive terms of BAS processes, former labels from Krupić, Corr et al. (2016) are placed in brackets. In addition, Berridge and Robinson's (2003) labels 'wanting' and 'liking' corresponds to the definition of incentive motivation and liking, respectively; *Fun Seeking only partially represents of the wanting BAS process due to its too narrow content.

### 3.6.1 Structural studies investigating the reinforcement sensitivity theory

MRI has been used to correlate volume and structure of brain regions with r-RST personality traits (Reuter, 2008). A large study of n=430 (44-48 years of age) recruited from the general population, revealed a positive correlation between the BIS trait and overall hippocampal volume (Cherbuin et al., 2008). Also, positive correlations between the BIS and both the hippocampal volume and amygdala volume was found in a group of people experiencing pathological gambling (Rahman, Xu, & Potenza, 2013); a disorder with
overlapping phenomenology with TTM, such as impulsivity and shared involvement of the
fronto-striatal circuitry (Fineberg et al., 2010). Yet the opposite relationship was found in a
group of n=183 students. A negative correlation between harm avoidance, a feature of the
BIS, with grey matter volume of the hippocampus was reported (Yamasue et al., 2018).
These correlational relationships support the proposition that the septo-hippocampal system
is where behavioural conflict is intensified, the central function of the BIS (Gray &
McNaughton, 2000), and that the volume of the hippocampus may influence this trait.

No relationship between the BIS with hippocampus and amygdala grey matter
volume was found when n=114 adult males of a wide age range were subjects of an MRI
study (Fuentes, Barrós-loscertales, Bustamante, & Rosell, 2012). Counter to the evidence
above, these findings do not support the idea that volume of the amygdala and hippocampus
contribute to BIS personality trait (Jeffrey Gray & McNaughton, 2000; Kennis et al., 2013).
Yet, the same study presented evidence of a negative correlation between the BIS and grey
matter volume of the orbitofrontal cortex and precuneus (Fuentes et al., 2012), providing
evidence supporting a different aspect of r-RST. According to r-RST, the prefrontal cortex,
which includes the orbitofrontal cortex, underlies all three behavioural systems (figure 3.1);
the FFFS (the ventral prefrontal cortex), BIS (the dorsal prefrontal cortex) and BAS (Kennis
et al., 2013; McNaughton & Corr, 2008). Overall, the brain regions found within MRI
studies have some resemblance to, but does not fit neatly into, the neuropsychological
hierarches proposed within the r-RST (Kennis et al., 2013; McNaughton & Corr, 2008),
nevertheless associations between brain volumes and personality traits continue to be made.

Adding another layer of complexity are the findings that grey matter volumes
associated with the BIS and BAS differ between men and women (Li et al., 2014). A
negative correlation between BIS and grey matter volume of the left parahippocampal gyrus
was found in women, but in men this was a positive correlation. Again when grey matter
volume of the ventromedial prefrontal cortex and inferior parietal lobe were correlated with the BAS, women demonstrated a positive correlation, while men demonstrated a negative correlation (Li et al., 2014). A negative correlation was also found between the BAS, measured by the sensitivity to reward scale, and grey matter volume of the striatum in men (Barros-Loscertales et al., 2006). In adolescent women, the orbitofrontal cortex volume predicted sensitivity to threat (BIS), but not in men (Urosevic, Collins, Muetzel, Lim, & Luciana, 2012). Generally, these findings tend to support the neuropsychological hierarchies presented by Kennis et al. (2013) and behavioural and trait differences between gender. On scales purpose made to measure RST personality traits and behaviours indicate that males score higher on fight, reward expectancy, sensitivity to reward, and appetitive emotion. Females score higher on approach and reward responsiveness (Torrubia, Avila, & Caseras, 2008). As TTM tends to be more severe, chronic and common in women (section 1.2), gender differences in grey matter volume may be an underlying predisposition to TTM. Another overlap between the presentation of TTM and RST structural imaging studies is that of age of onset. Most commonly TTM begins around puberty (section 1.3). Increases in reward sensitivity was found during a two year period in adolescents that was predicted by left nucleus accumbens and orbitofrontal cortex volumes (Urosevic et al., 2012).

3.6.2 Functional studies investigating the reinforcement sensitivity theory

It has been argued that functional imaging is a more direct test of responsivity to rewarding and punishing stimuli that underlie or mediate the behavioural systems of approach and avoidance. Measures of brain responsivity, i.e. blood oxygenation-level dependent, to rewarding and punishing stimuli may underscore individual differences and allow prediction of personality traits and behaviour (Smillie, 2008). fMRI studies typically use behavioural tasks and emotional stimuli to correlate areas of brain activation with RST personality measures. This allows interpretation of data across motivation, cognition,
emotion, biology and behaviour (Martin Reuter, 2008; Smillie, 2008). The use of emotional and behavioural stimuli are appropriate to identify brain activation because specific emotions and behaviours occur in response to reward and punishment, which are grouped within the BIS, BAS and FFFS.

3.6.2.1 Discussion of functional imaging results associated with punishment, personality traits and behavior

There is a growing body of evidence supporting the link between brain function in response to punishing stimuli with the broad personality traits associated with punishment of the RST. This is operationalised by the BIS and Sensitivity to Punishment (SP) trait questionnaires (Carver & White, 1994; Kennis et al., 2013; Torrubia et al., 2001). Using a monetary incentive delay task, the involvement of the amygdala and hippocampus in processing punishing stimuli (anticipated monetary loss) has been confirmed (Hahn et al., 2010). Functional connectivity between the amygdala and hippocampus positively correlated with the personality trait of sensitivity to punishment (Hahn et al., 2010).

Conflict is a central motivating factor of the BIS, and can be operationalized by stimuli or tasks that embody conflict. When an emotional stroop task was completed by participants (n=39), with conflict being the incongruence between facial expression and text, the amygdala and subgenual anterior cingulate were activated (Haas, Omura, & Constable, 2007). This finding supports the neuropsychological hierarchy of the BIS (Kennis et al., 2013) and agrees with research demonstrating that the amygdala and anterior cingulate processes punishing stimuli (Kennis et al., 2013). Further, activation of these brain areas correlated with the personality trait neuroticism, with the anxious form of neuroticism being more important than the depressive form of neuroticism in explaining variance of activation (Haas et al., 2007). The emphasis of anxious rather than depressive type of neuroticism
closely reflects theory, in which the BIS associated with anxiety, increases level of arousal and attention (McNaughton & Corr, 2008, pg. 78).

Attentional control and cognitive load on brain activity on levels of BIS have been explored in n=30 individuals, aged 18 to 65 (Bunford, Roberts, Kennedy, & Klumpp, 2017). Participants scoring high in BIS had higher dorsolateral prefrontal activity during a letter matching task when distracted by angry faces, and also, higher activity of the dorsal anterior cingulate cortex when distracted by fearful faces (Bunford et al., 2017). The angry and fearful faces in the study were used as threatening distractors and those scoring high on the BIS scale had higher activation of BIS associated brain regions when these distractors were presented. Higher activation of these brain regions indicated a higher sensitivity to threatening stimuli. The central element of the BIS, conflict, was operationalised in Bundord et al (2017) as between cognition and emotion, rather than between combinations of approach and avoidance behaviour.

It has been found that in a group of healthy participants (n=24), the BIS, rather than BAS personality trait was more influential on brain activity that occurred in response to emotional stimuli. This was the case using the International Affective Picture System, regardless of whether brain activation was in response to disgust, fear or erotic images (Reuter et al., 2004). Many activated brain regions correlated with BIS when activation was in response to disgust; cingulate, amygdala, and thalamus. Fear correlated with the cingulate and thalamus. Erotic images correlated with the cingulate, thalamus, amygdala, insula, basal ganglia, and brain stem. Whereas, only activation of the insula in response to disgust, and the hippocampus in response to erotic stimuli were correlated with BAS scores (Reuter et al., 2004). The authors concluded that many of these activated structures did not fit existing r-RST theory but that the BIS/BAS personality dimensions were able to identify differences in processing of emotional stimuli (Reuter et al., 2004).
3.6.2.2 Discussion of functional imaging results associated with reward, personality traits and behaviour

The ventral striatum, a core brain area of the BAS (Kennis et al., 2013) has been found to respond to a number of rewarding stimuli (Mortensen, Lehn, Evensmoen, & Håberg, 2015; Simon et al., 2010). A priming task, in which reward was operationalised as the successful completion of a trial, activated the ventral striatum (left caudate and accumbens). In accordance with RST, high scores on sensitivity to reward, measured by the Sensitivity to Punishment and Sensitivity to Reward Questionnaire (SPSRQ), were associated with increased ventral striatum activation (Mortensen et al., 2015). Not only did the data confirm the underlying neuropsychological hierarchy of the BAS, it also provided support for the notion that activation of the three behavioural systems, BIS, BAS and FFFS influence and can be relative to each other (Corr, 2001). Sensitivity to reward scores adjusted for levels of sensitivity to punishment was a better predictor of ventral striatum activation than sensitivity to reward alone (Mortensen et al., 2015).

The influence of a rewarding experience on brain activation has also been explored using a monetary incentive delay task (Simon et al., 2010). The task divides reward into two types: actual reward, also known as capturing of a reward and consummatory reward (Corr, 2004; Krupić & Corr, 2017); and anticipatory reward, which is closely related to motivation (Corr, 2008; Gard et al., 2006; Krupić & Corr, 2017). Ventral striatum activation was noted in response to anticipatory reward and activation of the medial orbitofrontal cortex was found in response to consummatory reward (Simon et al., 2010). When these activated areas were correlated to questionnaire data, as expected, it was found that those with high activation in response to reward in both regions were also reported high BAS scores (Simon et al., 2010).
Another monetary based reward task, also approximating the experience of consummatory reward, requires the participant to guess whether a number is higher or lower than 5; if correct they win money as a reward. A positive correlation between BAS-drive and dorsomedial striatum (caudate nucleus and putamen) activation was found in response to reward with this task (Costumero, Barrós-loscertales, & Fuentes, 2016). The BAS-drive personality trait has been described as goal-achievement, it is also known as ‘striving’ (Krupić & Corr, 2017). Overall, it was concluded that reward is processed by the dorsomedial striatum, the ventral striatum and medial prefrontal cortex; whilst the experience of punishment is processed by the insula and cingulate cortex. Within this monetary based gambling task the punishment condition was the loss of money if an incorrect guess was made (Costumero et al., 2016). Thusly, studies using reward and punishment conditions can explore associated underlying neural networks of reward and punishment based personality traits (Costumero et al., 2016; Simon et al., 2010).

A go no-go task measures the ability to inhibit an automatic behavioural response to a cue. They are usually thought of as a measure of impulse control or impulsivity, with poorer performance on the task demonstrating higher impulsivity, this is the usual reason go no-go tasks have been used in TTM research (Bohne, Savage, Deckersbach, Keuthen, & Wilhelm, 2008; Chamberlain et al., 2007). Within RST the data from the go no-go task can be thought of as related to both the BIS and BAS. It has been argued that go no-go tasks present an approach-avoidance conflict of the BIS (Collins et al., 2017). Yet, high impulsivity has been associated with BAS and reward sensitivity (Corr, 2004; Torrubia et al., 2001). A positive relationship between reward sensitivity with behavioural data from the go no-go task, and activation of the inferior frontal gyri has been reported (Fuentes-claramonte et al., 2016). Evidence was also presented demonstrating that reward sensitivity mediated the relationship between activity of the inferior frontal gyri and reaction time.
variability of the go no-go task (Fuentes-Claramonte et al., 2016). These findings indicate that high trait reward sensitivity is an important driver of impulsivity, a behaviour previously argued as central to TTM (Grant et al., 2007).

3.7 Conclusions

The reviewed imaging research, MRI and fMRI, was used to define and test the underlying biology of RST. There is a push for more such research to be done (Krupić & Corr, 2017; Martin Reuter, 2008), even though a substantial body already exists, see Kennis et al. (2013). The integration of RST and neuroimaging research is now essential, as neuroimaging may allow researchers to predict personality form brain structure and function (Collins et al., 2017; Smillie, 2008). A limitation to keep in mind with existing imaging studies is their use of the BIS/BAS scale. This scale does not separate the BIS (anxiety) and FFFS (fear), as postulated in the r-RST, but rather, measures a predisposition to anxiety and punishment sensitivity (Carver & White, 1994). Many brain regions were correlated with the RST personality scales of BIS/BAS and SPSRQ. For this reason, the use of these scales may go some way in helping identify the underlying driving motivation of hair pulling. They may also help uncover how personality traits are associated with brain function in those who pull their hair. That is, whether people who engage in hair pulling behaviour are high or low in sensitivity to rewarding or punishing stimuli, and if there are neural correlates that underpin them.
4 The relevance of reinforcement sensitivity theory to trichotillomania
The prominent role of arousal, reinforcement, avoidance, reward and punishment processes posited within the models of TTM (section 2) are crucial ideas in the development of RST (Corr, 2002; Corr & McNaughton, 2008; Heym, Ferguson, & Lawrence, 2008). Most importantly, the r-RST integrates research from a biological and personality perspective (Collins et al., 2017), typically separated in the TTM literature. No studies have been identified that investigate the relationship between personality and brain function in a cohort of individuals with TTM. In this chapter evidence from various levels of enquiry - neuroimaging, neuropsychological, psychological and personality – are used to argue the relevance of RST to TTM.

4.1 Reward, personality and imaging in trichotillomania

Impulsive behaviour is driven by the desire to approach rewarding stimuli; one’s propensity to respond to reward is sensitivity to reward (McNaughton & Corr, 2004; Smillie, 2008). As was presented in table 3.3, pg. 58, sensitivity to reward and BAS correlates with Extraversion, Agreeableness, Openness to experience and Conscientiousness of the five factor model (Krupić & Corr, 2017). In those with TTM, high openness to experience lower agreeableness in combination with high neuroticism was associated with greater symptom severity (Keuthen, Tung, Altenburger, et al., 2015). The neural processing of reward in TTM may underlie these personality factors. Decreased nucleus accumbens activation in those with TTM was reported for anticipatory reward, and over-activity of the nucleus accumbens was reported for actual reward (White et al., 2013).
4.2 Punishment, personality and imaging in trichotillomania

TTM shares its diagnostic category with OCD due to overlapping similarities. In r-RST compulsive behaviour is driven by the motivation to reduce distress and avoid punishment, as are the compulsions in OCD. One’s propensity to respond to punishing stimuli is sensitivity to punishment and drives the BIS and FFFS (McNaughton & Corr, 2004; Smillie, 2008). Within the five factor model of personality sensitivity to punishment, FFFS and BIS correlates with neuroticism (Corr, 2016). Those with TTM experience high levels of neuroticism (Keuthen, Tung, Altenburger, et al., 2015) and over-activity of the nucleus accumbens in response to punishing stimuli (White et al., 2013).

4.3 How defensive direction relates to trichotillomania

As explicated in section 3.1, in the r-RST, behavioural response to punishment is divided into defensive direction. The two directions being, the active avoidance of a dangerous situation eliciting fear, and the approach to a dangerous situation eliciting anxiety (Blanchard & Blanchard, 1989; McNaughton & Corr, 2004). For example, abruptly exiting a room in response to cruel remarks around their hair loss could demonstrate active avoidance and fear; re-entering the room may be an approach to what is perceived as a dangerous situation eliciting anxiety. This example is supported by qualitative (Casati et al., 2000) and quantitative research in TTM (Marcks et al., 2005) indicating social ostracism, negative evaluation and stigma can be problematic in TTM. Given that healthy individuals experience increased approach to threat when high in trait anxiety (Perkins & Corr, 2006), and those with TTM tend to experience high trait anxiety (Diefenbach, Tolin, Hannan, Crocetto, & Worhunsky, 2005), it follows that those with TTM may be predisposed to approach threat rather than avoid it.
4.4 How defensive distance relates to trichotillomania

Intensity of behaviour in those with TTM may vary according to the immediacy of a threat, i.e., attack at a small defensive distance, or flight and freezing when further away from the threat (McNaughton & Corr, 2004). Attack, or feeling like lashing out at others, might occur in TTM if one’s hair loss is about to be involuntarily exposed in public, as described by Michael (2004). Behavioural freezing may occur in the same situation should the individual not be able to leave. The perceived defensive distance would seem shorter to someone with severe hair loss due to TTM than someone with no experience of TTM, recall table 3.2 pg. 48.

Defensive distance may help us organise existing knowledge of TTM. TTM has long been thought of as a habit-like disorder involving little cognitive and executive influence (Azrin et al., 1980). Should this be the case we would expect periaqueductal grey, hypothalamus, and amygdala involvement in TTM as these brain regions are associated with small defensive distances. More recently cognition has become the focus of research (Chamberlain, Grant, Costa, Müller, & Sahakian, 2010; Keijsers, Maas, Opdorp, & Minnen, 2016; Norberg et al., 2007). The greater the influence of cognition in TTM, the greater we would expect the role of the cingulate and prefrontal brain regions. As these brain regions are associated with large defensive distance.

The periaqueductal grey is associated with a very short defensive distance (Kennis et al., 2013). At the most basic level, in the brain stem, the periaqueductal grey carries messages of pain to the brain. Counter to the biopsychosocial model of TTM, the attenuation of pain in TTM has not been supported (Blum et al., 2017). Although, other areas associated with short defensive distance have been. Abnormal grey matter abnormalities of the left amygdala have been found in those with TTM using morphometric MRI (Chamberlain et al., 2008). Also fMRI conducted during resting state, has found decreased activation from the
right basolateral amygdala to the orbitofrontal cortex was found in those with TTM (White et al., 2013). While no correlations with symptom severity were reported, these areas have been shown to differ in TTM compared to healthy controls.

4.5 How the behavioural inhibition system relates to trichotillomania

The septo-hippocampal system, posterior cingulate cortex, and dorsal prefrontal cortex process the more complex and cognitive elements of the BIS (Kennis et al., 2013; McNaughton & Corr, 2004). The septo-hippocampal system is made up of the sub-areas CA1 and CA3 of the hippocampus, the subiculum, locus coeruleus, entorhinal cortex, amygdala, periaqueductal grey, medial and lateral septum, and mammillary body (Gray & McNaughton, 2000). A fMRI study from Rauch and colleagues (2007) did not support a role of the septo-hippocampal system in TTM when a serial reaction time task was used as a stimulus. Yet grey matter density abnormalities may be apparent within the system (Chamberlain et al., 2008). It could be argued that the dorsal prefrontal cortex of the BIS is relevant to TTM, as the same study (Chamberlain et al., 2008) also reported grey matter abnormalities of the frontal superior cortex. Further, abnormal activity in the dorsal prefrontal region, was reported in the left mid-posterior frontal area, which was found to correlate with symptom TTM severity (Stein et al., 2002).

A number of neuropsychological tests have shown poor divided attention in TTM sufferers (Stanley, Hannay, & Breckenridge, 1997). Impaired divided attention in TTM may theoretically relate to the BIS, i.e. the resolution of a conflict, which may require the splitting of attentional resources between competing goals (McNaughton & Corr, 2004). Together reward and punishment, and goal conflict, work to increase arousal resulting in BIS behaviours (McNaughton & Corr, 2008) that may underlie the struggle controlling
one’s hair-pulling (Rehm et al., 2015). Impulsive behaviour is influenced by arousal (Dickman, 2000), and the BIS increases arousal to resolve conflict. This idea is analogous to the stimulus regulation model of TTM (Penzel, 2008) and the ethological model of TTM (Swedo, 1989), in which level of arousal is central. The decision mechanism, presented in figure 4.2, could be used to explain approach and avoidance of hair-pulling. Within the BIS this conflict elicits the emotional response of depression and anxiety, depression and anxiety are often comorbid with TTM, although recent research points to an emphasis on anxiety rather than depressive disorders (Grant et al., 2017).

![Figure 4.1 Effects of motivational systems on arousal and decision, McNaughton and Corr (2008)](image_url)
4.6 How the fight, flight, freeze system relates to trichotillomania

The BIS resolves conflict with a bias favouring avoidance, which is the behaviour associated with the FFFS if the threat is avoidable. Fight and freeze behaviours occur if the threat is unavoidable. The avoidance of emotion, experiential avoidance, has been touted as driving the behaviour of hair-pulling (Begotka, Woods, & Wetterneck, 2004; Norberg et al., 2007). Psychological avoidance in the form of dissociation in TTM has also been identified (Lochner et al., 2004). Behavioural avoidance in TTM has been described as covering bald spots and limiting intimacy to avoid negative social evaluation (Bornstein & Rychtarik, 1978; Casati et al., 2000). The experience of panic, a tendency to freeze or become aggressive has also been described (Bouwer & Stein, 1998; Javidi, Battersby, & Forbes, 2007).

The FFFS is activated in response to punishing stimuli and functions to move the organism away from it. A stimuli that elicits avoidance, panic and fear may derive from learning and knowledge (Corr & McNaughton, 2008). Examples of threat in TTM could be: learning that having bald patches is socially unfavourable; judging a kinky hair as defective; interpreting the appearance of a bald spot as proof of being a bad person; or viewing someone as a threat to self-esteem because they have long thick hair; or the behaviour of hair pulling itself could be a punishing stimulus (Bornstein & Rychtarik, 1978; Bouwer & Stein, 1998; Casati et al., 2000; Javidi et al., 2007). The threat may be perceived as avoidable or unavoidable, constituting the stimulus condition, recall table 3.1 pg. 45, in which the response to avoidable threat is fear and escape, and the response to unavoidable threat is panic, fight and freeze. For example, an individual with TTM may believe that the distressing behaviour of hair pulling and the urge to perform it is unavoidable (Ferrão et al., 2006), in which case, one would respond to the behaviour with feelings of panic and behaviours of aggression. Should the individual believe that the urges and behaviour are
avoidable, r-RST tells us that they will respond to hair pulling with fear and avoidance behaviour.

Indeed, in TTM a picture of hair may stimulate the FFFS, resulting in avoidance behaviour such as shifting attention away from the picture. Lee, Franklin, Turkel, Goetz, & Woods, (2012) found that a picture of hair influenced attentional disengagement in those with TTM. Those with TTM showed heightened disengagement in late attentional processing (1500ms) in response to hair related cues. The authors explained their findings on the need for those with TTM to regulate negative emotional responses to the hair cues once the cues reached conscious awareness, in line with the FFFS. Attempts to integrate research on attention, imaging and r-RST personality traits are already being made (Collins et al., 2017). This integration may help form a multi-level understanding of TTM that includes existing knowledge of imaging literature.

A number of brain regions implicated in TTM overlap with the areas included in the FFFS. The anterior cingulate and dorsal prefrontal cortex are placed within the defensive avoidance hierarchy (McNaughton & Corr, 2008). Evidence implicating the anterior cingulate has been found in TTM. Decreased connectivity of the dorsal anterior cingulate to the NAcc was found in individuals with TTM (White et al., 2013), as well as reduced white matter integrity between the orbital frontal cortices and anterior cingulate cortices (Chamberlain, Hampshire, et al., 2010). The prefrontal cortex has shown to have volume (Grachev, 1997) and grey matter anomalies in TTM (Chamberlain et al., 2008). Further, the function of the left mid posterior and left superior lateral frontal areas correlated with severity measures (Stein et al., 2002). The FFFS is an idea that draws together multiple levels of research; attentional, affective, cognitive, behavioural, functional and structural brain imaging. This evidence indicates that the FFFS may be a relevant concept to TTM.
4.7 How the behavioural activation system relates to trichotillomania

The motivation and execution of impulsive behaviours are more complicated than a simple reaction to reinforcing stimuli in RST. The role or purpose of the BAS is to move the organism closer in time and space to the final biological reinforcer (Corr, 2004). Within the BAS system, and particularly in humans, sub-goal scaffolding occurs, a type of problem solving that begins with identifying the biological reinforcer; develops to planning the behaviour; and finalises by enacting the plan (Corr, 2008). The biological reinforcer that motivates an individual to approach reward in TTM may be the actual removal of a hair. That increases behaviours such as seeking and identifying the perfect hairs to pull out (Rehm et al., 2015); this would involve using restraint and planning to target the ‘right’ hairs (Keuthen & Sprich, 2012). Such behaviour may reflect the notion of sub-goal scaffolding. Sub-goal scaffolding may also be used to some extent to restrain the hair pulling behaviour until the individual is alone (American Psychiatric Association, 2013).

Impulsiveness is important within the BAS when goal capture is imminent (Corr, 2008). Those with TTM have described their hair-pulling experience as an “escalating sense of urgency to achieve gratification as the hair pulling episode continued” (Rehm et al., 2015, p. 21). This description seems to capture the idea of consummatory pleasure rather than anticipatory pleasure. An emphasis on consummatory pleasure in TTM was indicated by the results of an in-depth investigation into impulsivity and compulsivity using various questionnaires (Ferrão et al., 2006) and a neuropsychological test of motor inhibition, the stop-signal reaction time task (Chamberlain, Fineberg, et al., 2006; Odlaug et al., 2014).

As noted in table 3.3 pg. 58, there are many overlapping ideas between the BAS and neuroimaging paradigms. It follows that overlap may be found with imaging research in TTM. The ventral striatum consists of the nucleus accumbens (NAcc) and the olfactory tubercle, and has been proposed to be a core element of the behavioural approach hierarchy
in r-RST. Within this hierarchy, the NAcc was allocated the central task of selecting and organising goals to carry out a motor program (McNaughton & Corr, 2008). Given the central feature of TTM is a motor pattern of plucking out a single hair, which is often repeated thousands of times, it is not surprising that evidence has been found in the imaging literature linking the NAcc to TTM (White et al., 2013). Not only has activation and connections of the NAcc found to be different to healthy controls, but also both left and right NAcc have been found to correlate with TTM symptom severity, when measured by the Yale Brown Obsessive-Compulsive Scale (Roos et al., 2015).

While not considered a core element of the BAS, as it does not play a role in goal selection, the dorsal palladium facilitates communication between other areas (McNaughton & Corr, 2008). The dorsal palladium and putamen together form the lenticulate. Those experiencing TTM were shown to have decreased left lenticulate volumes and decreased left putamen volumes compared to healthy controls (O'Sullivan et al., 1997). Also peripheral to the core BAS system is the dorsal striatum, made up of the caudate nucleus and putamen (Corr & McNaughton, 2008). A number of studies using various imaging methods show evidence that the putamen may play a role in TTM (Chamberlain et al., 2008; Stein, van Heerden, Hugo, et al., 2002; O'Sullivan, Rauch, Breiter, Grachev, et al., 1997; White et al., 2013). Further, the caudate has been found to correlate with TTM symptom severity (Stein et al., 2002; Swedo et al., 1991). Also found to correlate with TTM severity was white matter integrity of the internal capsule. The internal capsule projects through the caudate nucleus and putamen, relays sensory and motor information from the cortex to the brainstem, and extends as the corona radiata. White matter integrity of the internal capsule, which passes through the ventral and dorsal striatum, were positively correlated with symptom severity (Roos, Fouche, Stein, & Lochner, 2013).
4.8 How constraint relates to trichotillomania

Constraint is a top down personality trait that exerts control over the other behavioural systems. Constraint would be required to resist the tendency to approach reward, e.g., overcome the urge to pull hairs that do not meet the individual’s idea of the ‘right’ hair, and resist the urge to pull hair in front of other people. Constraint would also be needed to overcome avoidance of punishment, e.g. forcing oneself to attend a social occasion even though ridicule over having no eyes brows is expected. Low constraint may contribute to poor control over divided attention (Stanley, Hannay, & Breckenridge, 1997) and the inability to consciously control one’s behaviour and impulses to pull out hair. Constraint involvement may also explain why those with TTM experience a sense of mastery when achieving a goal associated with hair-pulling (Geisser & Rizvi, 2014) and why beliefs around control in those with TTM are deemed important (Rehm et al., 2015).

Constraint is largely seated in the prefrontal cortex and anterior cingulate cortex. A number of studies have found evidence for frontal lobe or prefrontal cortex involvement in TTM. There is mixed evidence about frontal volumes in TTM compared to controls, with decreased volumes (Grachev, 1997), greater cortical thickness (Odlaug et al, Chamberlain, Derbyshire, Leppink & Grant, 2014), or no difference at all (Stein et al., 1997) being reported. Increased grey matter density has been found in frontal areas (Chamberlain et al., 2008), as has reduced white matter integrity (Chamberlain, Hampshire, et al., 2010). The level of white matter integrity correlated with symptom severity in a number of frontal areas (Roos et al., 2013; Stein et al., 2002).
4.9 Summary

The usefulness of investigating TTM based on RST is not only conceptual but practical. Almost no literature has been identified that measures response to reward and punishment in a TTM cohort. In fact, literature that defines sources of reward and punishment (the stimuli) in TTM are limited (Casati et al., 2000; Marcks et al., 2005; Rehm et al., 2015). RST has purpose made self-report trait measures for the degree of reward and punishment one perceives and responds to, these can be used regardless of whether stimuli are defined (Carver & White, 1994; Jorm, Christensen, Henderson, Jacomb, Korten, & Rodgers, 1999; Torrubia et al., 2001). However, to date no research has used these measures to examine reward and punishment in TTM.

In summary, hypothetical examples have been given of how RST may be used to make sense of TTM, it is now imperative to explore whether data endorses or challenges the relevance of RST to TTM. Differences in sensitivity to rewarding and punishing stimuli are reflected in personality, whereby short term state responses influence long term trait dispositions (Gray & McNaughton, 2000; Gray, 1987; Pickering & Corr, 2002; Smillie, 2008) this may extend to TTM. Conceptualizations of TTM neglect the role of motivation, and typically have been proposed with minimal supporting data. If RST is found to be applicable to TTM the question of what drives the behaviour of hair pulling may be addressed more directly based on reward and punishment. RST brings together two areas of research that of neural processes and personality (Corr & McNaughton, 2008; Smillie, Pickering, Jackson, Pickering, & Jackson, 2006) making RST an appropriate and relevant theoretical framework to make sense of TTM as contemporary research struggles to reconcile neurobiological findings with its presentation (Chamberlain, Odlaug, Boulougouris, Fineberg, & Grant, 2009; Fineberg et al., 2010; Flessner et al., 2012).
STUDY 1. How reward and punishment are viewed by individuals experiencing trichotillomania according to the revised reinforcement sensitivity theory

Published as:


See APPENDIX A for ethics approval

See APPENDIX N for the Qualitative Interview Guide

See APPENDICS E, L and M for the scales MGH, DASS and NIMH-TS respectively.

See APPENDIX Q for authorship from

See APPENDIX V for copyright agreement
6. STUDY 2. Types of avoidance in hair-pulling disorder (trichotillomania): an exploratory and confirmatory analysis

Published as:


See APPENDIX B for ethics approval for Study 1 and 2.
See APPENDIC S E, I, J, and L for the MGH, CBAS, AAQ, and DASS respectively.
See APPENDIX O for supplementary material published with the manuscript,
See APPENDIX W for copyright agreement
See APPENDIX R for authorship form
7 STUDY 3. Motivation underlying hair-pulling behaviour conceptualized by the reinforcement sensitivity theory

Published as:

APPENDIX B ethics study 1
APPENDIX C ethics study 2
APPENDIX D ethics study 3

See APPENDIX K, APPENDIX E, APPENDIX G, APPENDIX F, for the respective scales DASS, MGH, BIS/BAS and SRSPQ

APPENDIX S for authorship form
8 STUDY 4. A systematic review of published primary studies of neuropsychology and neuroimaging in trichotillomania

Published as:


See APPENDIX P for a list of screened abstracts with reasons for exclusion

See APPENDIX X for Copyright agreement

See APPENDIX T for Authorship form
9 STUDY 5. Reward and punishment in trichotillomania: fMRI and self-report evidence

This study was under review when the thesis was released to the public, please contact authors for further information.

See APPENDIX D for ethics approval

See: APPENDIX E, APPENDIX L, APPENDIX K, APPENDIX F and APPENDIX G for the MGH, TIS and TSS, DASS, SPSRQ and BIS/BAS scales respectively

See APPENDIX M for a figure of the gambling task

See APPENDIX U For authorship indication form
10 Discussion
The results of the five studies have been presented and discussed separately within each publication. So as not to repeat information already presented, the discussion begins with an overarching description of how findings from all studies can be made sense of, and interpreted within r-RST and the interaction between the behavioural systems, section 10.1. Within section 10.1 study results are summarised into a motivational model of TTM. Overarching results are then discussed and presented within each of the behavioural systems. Trait sensitivity to punishment is discussed within the FFFS because within r-RST only punishing stimuli activates the associated neurological network leading to avoidance behaviours, section 10.1.1. Trait sensitivity to reward is discussed within the BAS because within r-RST only rewarding stimuli activates associated neurological networks leading to behavioural approach to reward, section 10.1.2. Goal conflict, regardless of reward and punishment is the trigger for BIS associated neural networks and behaviours, section 10.1.3. Discussion and interpretation of findings within the behavioural systems are organised in a bottom up fashion, i.e., biological to psychological elements, this structure is used within the figures summarising each of the behavioural systems in TTM, figures 10.2, 10.4 and 10.5.

Implications for understanding the role of reward and punishment as underlying motivation are discussed in section 10.2; implications for clinical practice are discussed in section 10.3, and implications for further research are discussed in section 10.4. Section 10.5 presents the limitations and strengths of the research as a whole. Conclusions are finally given in section 10.6.
10.1 Integration of study findings based on r-RST

Studies herein supported the notion that those with sub-clinical levels of hair-pulling experience high levels of both trait reward and punishment sensitivity when self-report measure are used (study 3). However, once TTM symptoms become clinically relevant punishment becomes the predominate motivation. Those with TTM experience high trait sensitivity to punishment and abnormal biological activity of the striatum in response to reward, measured using fMRI (study 1, 3 and 5). Yet, the experience of pleasure was not completely absent in those with TTM or sub-clinical hair-pulling, rather reward was described as being limited to hair-pulling.

Within this section study results have been organised in two ways to assist interpretation, both within the frame work of r-RST. Firstly, overarching results are interpreted across behavioural systems, BIS, BAS, and FFFS (figure 10.1), as the behavioural systems influence each other depending on their function, explained in sections 3.2 to 3.5. Secondly, the behavioural systems span multiple levels of enquiry and the overarching results illustrate how the behavioural systems manifest across those levels (table 10.1). The same results are presented in figure 10.1 and table 10.1, but organised differently to demonstrate the two ways of interpreting the overall findings. Both ways of interpreting the data are used together in this section with the aim to provide a brief overview of r-RST in TTM.
Figure 10.1 Relationship between stimuli, the FFFS, BAS and BIS in clinical hair pulling disorder (blue), imposed on a diagram from McNaughton and Corr, 2004, pg. 78 (black).
**Table 10.1 Synthesis of evidence from studies 1, 2, 3 and 5 across the levels of emotion, behaviour, motivation, stimuli and constraint.**

<table>
<thead>
<tr>
<th>Emotion/state</th>
<th>Self-report evidence (study 3)</th>
<th>Qualitative description (study 1)</th>
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<tbody>
<tr>
<td></td>
<td>Depression and sensitivity to punishment significantly separates controls, sub-clinical and clinical TTM</td>
<td>BIS emotion/state - Anxiety and worry, Depression and rumination, FFFS emotion - Fear, Trance and dissociation, BAS emotion - Anticipatory pleasure, Unattainable pulling and anger, towards loved ones</td>
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<tr>
<th>Behaviour</th>
<th>Quantitative description of avoidance (study 2)</th>
<th>Qualitative description (study 1)</th>
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<tr>
<td></td>
<td>Five types of avoidance increase with level of symptom severity</td>
<td>BIS behaviours - Risk assessment, FFFS behaviours - Escape, Avoidance, Hair-pulling as avoidance, Self-protection, BAS behaviours - Sub-goal scaffolding and pulling alone, Exploration of individual hairs</td>
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<tr>
<th>Motivation</th>
<th>Self-report evidence (study 3)</th>
<th>Self-report and fMRI evidence together (study 5)</th>
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<tbody>
<tr>
<td></td>
<td>Levels of sensitivity to reward and sensitivity to punishment together separates groups with and without sub-clinical symptoms</td>
<td>Increased striatal activation in response to reward may predict increased sensitivity to punishment</td>
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<tr>
<th>Motivation</th>
<th>fMRI evidence (study 5)</th>
<th>Qualitative description (study 1)</th>
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<td></td>
<td>Increased activation in the bilateral putamen and pallidum, and right caudate in response to rewarding stimuli in those with clinical hair-pulling</td>
<td>BIS conflict - To pull versus not pulling, Intimacy versus keeping hair-pulling a secret, Sensitivity to punishment - Views themselves as moderately-to-highly sensitive to punishment, Sensitivity to reward - Dismisses, minimises or views reward with distrust</td>
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<td>Rewarding Stimuli - Physical reward, Achievement/satisfaction, Reprieve from emotion, Punishing stimuli - Unattractive appearance, Social stigma, Distress around pulling episode, Low self-esteem, Loss of control</td>
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<th>Constraint/control</th>
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<td>Hair-pulling inhibition around others, Planned strategies to abstain, Perfectionistic pulling criteria, Ego depletion</td>
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<td>Disordered behavioural activation system and sensitivity to punishment in sub-clinical group</td>
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<th>Motivation</th>
<th>Self-report and fMRI evidence together (study 5)</th>
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| Qualitative description (study 1) | |
|----------------------------------| |
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For an organism to decide whether to approach or avoid a stimulus, inputs from the FFFS and BAS feed into the BIS, this process continues until the conflict is resolved (McNaughton & Corr, 2004), explained in 3.2. An example of how this idea applies to those with TTM can be presented based on our findings illustrated in figure 10.1. When deciding whether to engage in a hair-pulling episode an individual will experience the emotions of depression or/and anxiety, and risk-assessment behaviours (studies 1 and 3). Depression and anxiety are experienced in response to conflicting goals, in TTM this is chiefly a reward versus punishment conflict, described by participants as “battling the urge” where the rewards and punishments of hair pulling behaviour are in conflict (study 1). To resolve the conflict the individual engages in avoidance behaviours if the punishing stimuli hold more weight than rewards (studies 1, 2 and 3), or approach behaviours if rewards outweigh the punishments (study 1). The emotions, behaviours, motivation and stimuli central to the behavioural systems are discussed and presented in more detail in 10.1.1. to 10.1.3.

An individual’s level of trait sensitivity to reward and punishment can influence whether the outcome to conflicting goals results in an approach or avoidance reaction to stimuli, see section. According to r-RST the level of trait sensitivity to rewarding and punishing stimuli impacts the intensity of an individual’s response to stimuli (Corr & McNaughton, 2008). Those high in trait sensitivity to punishment tend to respond intensity to punishing stimuli because the defensive distance between them and the stimuli seem shorter than in actuality, recall section 3.1, table 3.2. Those with clinical levels of TTM have high levels of trait sensitivity to punishment (study 3 and 5) and a distrust of pleasure and reward (study 1) increasing the salience of punishing stimuli and resulting in a bias towards avoidance behaviour (study 1 and 2). Although the bias does not completely eliminate approach behaviours to reward (study 1). See the inputs into the FFFS and BAS for punishing and rewarding stimuli in TTM, figure 10.1.
According to r-RST, the relationship between stimuli and an individual’s level of sensitivity to reward and punishment, is mediated by biological functions (Corr, 2008) recall section 3.1. Abnormal over-activation of the bilateral putamen and pallidum, and right caudate in response to reward was found in those with TTM. Neural response (activation patterns) were a stronger predictor of TTM than personality measures of sensitivity to reward and punishment (study 5). There are a number of implications of these results including the implication that it is not a heightened biological response to punishment that is driving TTM. Rather, the dorsal striatum is working harder in those with TTM compared to healthy controls to process rewarding stimuli, attenuating the potential for reward as motivation in TTM. This interpretation is supported by a positive relationship between striatal activation and trait sensitivity to punishment (study 5) reflecting the notion that the behavioural systems do not work in isolation but they operate relative to each other and across levels of enquiry (Corr & McNaughton, 2008).

Participants have provided rich descriptions of TTM that reflect numerous conceptual ideas of r-RST (study 1). These conceptual ideas are the behavioural systems and individual variation on level of motivation to approach a reward and level of motivation to avoid punishment. Statistical evidence has demonstrated an association between trait sensitivity to reward and punishment, and TTM symptoms (study 2 and 3), and a relationship between the neural processing of reward (brain function) and trait measures (study 5). The findings presented in this thesis support the notion that RST is a relevant and useful theoretical construct in making sense of the motivation to pull out hair, a link not previously established. Overall the findings provide preliminary evidence for the role of key concepts from r-RST in TTM, which are elaborated below.
Our findings have added to the existing models of TTM. Striatal dysfunction (study 5) can be added to biological vulnerability towards TTM, building on the biopsychosocial model of TTM (Franklin et al., 2006). The r-RST is based on the ideas of defensive direction and defensive distance (3.1), rather than the notion of a conditioned stimuli as in the CBM (2.2), thereby, avoiding the problem of a circular argument and making the integration of our results a model of underlying motivation rather than a model of symptom maintenance. Our results are interpreted within a directional theoretical scaffold (figure 10.5). Findings from our qualitative study extended descriptions and added detail to a number of rewarding and punishing elements of the biopsychosocial model and CBM, (Franklin et al., 2006; Mansueto et al., 1999).

Arousal in the stimulus regulation model of TTM (Penzel, 2003) is either under-stimulated or over-stimulated based on predisposing biological contributions; hair-pulling restores arousal balance. Arousal within the current research was theoretically defined as arousal produced by goal conflict. In essence, the current findings address an area not previously explored in detail, that of motivation stemming from reward and punishment in TTM. Those with TTM are motivated to pull out hair due to a heightened sensitivity to, and broad experience of, punishment, and limited experience of reward. When all of the combined evidence is condensed, a model of motivation can be hypothesised, presented in figure 10.6.
**Figure 10.2 The motivational model of TTM**

- **a** Study 5. Underlying an increased sensitivity to punishment is the over activation of the bilateral putamen and pallidum, plus the right caudate in response to reward. Rather than subjectively experienced as reduced pleasure, an increased sensitivity to punishment is experienced.

- **b** Studies 3 and 5. High trait sensitivity to punishment has been repeatedly found in cohorts meeting clinically relevant TTM. Yet, this does not exclude pleasant and rewarding experiences in TTM altogether; rather, pleasure in TTM is restricted. High sensitivity to punishment exacerbates the five types of avoidance, depression and hair-pulling symptoms.

- **c** Study 3. When both high sensitivity to reward and high sensitivity to punishment occur, hair-pulling symptoms tend to be sub-clinical.

- **d** Study 2. A reliance on avoidance increases as hair-pulling symptoms increase, driven by high trait sensitivity to punishment.

- **e** Study 5. Depression becomes more important with increased hair-pulling symptoms, avoidance, and sensitivity to punishment.

*Not explored in the current series of studies*
10.1.1 Punishment and the flight, fight freeze system in trichotillomania

The FFFS was found to be the most influential of the behavioural systems in TTM. However, none of the neurobiological areas underlying the FFFS; periaqueductal grey, hypothalamus, amygdala, anterior cingulate cortex, and ventral prefrontal cortex (Corr, 2008; Kennis et al., 2013) demonstrated aberrant activation in our fMRI study. Even so, those with TTM still exhibited high trait sensitivity to punishment when measured as a personality trait. Those high in trait sensitivity to punishment tend to be hyper-aware of punishing and unpleasant stimuli, and have a strong emotional, behavioural and cognitive response to threat. Trait sensitivity to punishment underlies the trait of neuroticism (Corr, 2004), individuals with TTM tend to be high in both traits (Hagh-Shenas et al., 2004; Keuthen, Tung, Altenburger, et al., 2015).

In TTM punishing stimuli were described, such as having an unattractive appearance, and being exposed to social stigma and loss of control (study 1). Emotional and behavioural responses to these stimuli are exacerbated due to high trait sensitivity to punishment in those with TTM (study 3 and 5). Individuals with TTM are well aware this sensitivity (study 1). Within the FFFS responses to punishing stimuli occurred on a number of levels, such as: emotional, such as fear; cognitive processes, such as dissociation; and behavioural, such as escape (study 1). Five sub-types of avoidance were identified (study 2) and how avoidance occurs in TTM was described in detail by participants (study1). For further details see figure 10.2.
**Stimuli (study 1)**

Unattractive appearance. The appearance of hair loss was the most punishing aspect of TTM for participants. Participants repeatedly described baldness, thinning, patches, and being able to see their own scalp as “ugly”.

Social stigma and discovery of pulling. An awareness of hair-pulling as socially divergent was experienced as punishing, which in turn influenced how participants experienced how hair-pulling being discovered by others. Which was described as a particularly negative experience.

Distress during and after episode. High levels of distress during or after a hair-pulling episode as one of the worst aspects of their experience with TTM.

Low self-esteem. Participants described their inability to abstain from hair pulling as evidence that they are a “failure”. Perceptions of being physically unattractive or appearing “abnormal” contributed to participants’ low self-esteem and a sense of self-punishment.

Loss of control. Individuals either described hair pulling as a substitute for a lack of control in general life (i.e., it gave them a sense of control) or spoke about a lack of control over behaviour, attention and awareness as a negative experience.

**Emotion (study 1)**

**Fear** was described as an emotional reaction to the future possibility of one’s TTM and hair loss being discovered, and to the consequences of TTM (e.g., fearing loss of employment, negative social evaluation, post-pulling shame) by 50% of participants.

**Trance and dissociation.** To avoid distress, emotions, problems and decisions, the experience of dissociation or a trance-like state of mind was induced while pulling out hair for 37% of participants.

**Behaviour**

**Avoidance and attack (study 1)**

**Escape.** A recurring idea, fantasy or lifestyle choice was that of shaving one’s head to gain relief from the symptoms of TTM, and/or of re-locating to a new environment (e.g., overseas) to escape the stigma of hair loss and/or TTM. This idea was described by 44% of participants.

**Avoidance.** All participants explained that the behaviour of hair-pulling was a form of avoidance.

**Hair-pulling and stress** Hair-pulling behaviour served the function of reducing or coping with stress. Stressors ranged from significant life events (e.g., death of a loved one) to daily routines (e.g., child care, studying), and becoming aware of distressing emotions and thoughts in the absence of an external stressor (e.g., anxiety).

**Self-protection.** Within the FFFS, defensive attack occurs when a threat is perceived as imminent and unavoidable. Participants did not physically attack others when feeling threatened, but some (31%) described subtler behaviours and the need to psychologically prepare to defend themselves. Defensive attack was expressed verbally and with facial expressions.

**Personality trait – sensitivity to punishment (study 3 and 5)**

Groups with sub-clinical and clinical levels of symptom severity experienced heightened levels of trait sensitivity to punishment.

**Neurobiological contributions (study 5)**

The processing of punishing stimuli in TTM was not found to be different from healthy controls.

---

*Figure 10.3 Visual representation of the FFFS in trichotillomania*

Note: the FFFS has the most evidence supporting its involvement in trichotillomania.
10.1.2 Reward and the behavioural activation system in trichotillomania

The role of reward in TTM was less clear than that of punishment, trait sensitivity to reward was found to be important when symptoms were sub-clinical, but not when diagnostic criteria was met. Yet the detailed descriptions participants gave in our qualitative study, and the fMRI findings indicated that reward remains a salient influence in TTM. On the biological level, abnormal over activation of the striatum was found in response to reward, indicating that the neural processes involved in learning and habit formation may be disrupted. Our fMRI findings can be interpreted within the BAS neuropsychological hierarchy, figure 10.3, along with the findings of a previous fMRI study exploring reward and punishment in TTM; our findings are denoted by the red circles, whilst those of White et al. (2013) are denoted by the blue circle in figure 10.2 (McNaughton & Corr, 2004).
Figure 10.4 Gray's behavioural approach hierarchy (McNaughton & Corr, 2008, pg. 71) with relevant fMRI findings circled

Motor = Motor areas, DStr = dorsal striatum, DPal = dorsal pallium, VStr = ventral striatum, VPal = ventral palladium, VTA = ventral tegmental area, AC = anterior cingulate, Amyg = amygdala, VMH = ventro-medial hypothalamus, PAG = periaqueductal grey, red circles = results from our fMRI study, blue circle = results from White et al, 2013.
Within the BAS neuropsychological hierarchy some areas are responsible for prioritising and ordering motor programs pertaining to goal selection; see the middle column in figure 10.3, which represents the ‘BAS proper’. Other areas are also involved, but only support the ‘BAS proper’ by holding motor sub-routines; see the outside columns in figure 10.3 (McNaughton & Corr, 2008, pg. 72). Our findings span both the central and peripheral networks. Our fMRI results (study 5) and those of White et al. (2013) can be interpreted within the BAS hierarchy. They point to a disruption of the selection and processing of rewarding goals and the motor routines associated with them, rewarding goals, behaviours and motor routines were described in detail by participants (study 1).

Rewarding goals in TTM were described as physical sensations and a sense of achievement and satisfaction that trigger sub-goal scaffolding and exploration of individual hairs as approaches to hair-pulling behaviour in TTM. These behaviours are goal directed and complex, which would require exertion of control from the constraint system to perform, explained in sections 3.4 and 3.5. During these behaviours participants ‘looked forward’ to the pulling episode when hair pulling was available, or felt frustrated and angry if hair-pulling was unattainable, see table 3.1, for how stimulus conditions influence emotional states. It is concluded that in TTM it is the ‘how’ and ‘from where’ reward is experienced, i.e., reward associated with hair-pulling, rather than magnitude of how sensitive one is to reward in general, which is important in TTM.
Physical reward. Half of the cohort experienced rewarding and pleasant physical sensations. They were described as; the sensation of a hair leaving the skin, feeling the texture of an individual hair or many hairs with one’s fingers, addressing an allergen-type sensation by pulling out hair (i.e., similar to the scratching of an insect bite), and putting the hair in one’s mouth and biting it.

Pleasurable emotion as negation of punishment. The significance of pleasurable emotion in relation to hair-pulling was a reprieve from something unpleasant; described by 75% of the participants. One individual explained that hair pulling felt good because it took “the sting out of it…the pain, a bit like chocolate”.

Achievement/satisfaction. A sense of achievement and satisfaction was reported by 63% as the immediate reward after successfully pulling out the desired hair. This was experienced if it was physically difficult to remove, or if specific characteristics of the hair were judged as highly desirable to be rid of.

Anticipatory pleasure. Six participants described feelings of hope and anticipatory pleasure when looking forward to the appetitive stimuli described in previous themes (e.g., physical reward, achievement/satisfaction, and pleasurable emotion as negation of punishment).

Unattainable hair-pulling, anger towards loved ones. If the appetitive stimulus is unattainable rather than attainable, the BAS proposes that aggression can occur. For instance, when prevented from pulling by family members or friends, 50% of participants reported feeling frustration, anger, and aggressive verbal and body language.

Sub-goal scaffolding and pulling alone. Some individuals (31%) described deliberately leaving a room, waiting to be alone, or seeking out privacy to commence hair-pulling so as to avoid prevention of, or interruption during, their hair-pulling behaviour.

Exploration of individual hairs. Participants (62%) described exploring individual hairs with their attention continually and repeatedly being focused on one hair at a time, plucking the desired hairs out as they explore. During the exploration of hair, participants would inspect the hairs (visually or with the fingers) to judge whether it was a “good” one to pull out.

Personality trait – sensitivity to reward

(study 3) High trait sensitivity to reward for sub-clinical hair-pulling

(study 1) Rejection of reward and pleasure outside of hair-pulling

Neurobiological (study 5)

Over activation of bilateral putamen and pallidum, and left caudate in response to reward

Figure 10.5 Visual representation of the BAS in trichotillomania
10.1.3 Goal Conflict and the behavioural inhibition system and trichotillomania

No evidence was found linking neural structures associated with the BIS to TTM. Yet, the BIS is activated by conflicting goals. Conflict between the biological and personality levels of response to stimuli were found with overactive striatal activation in response to reward and high trait sensitivity to punishment (study 5 and 3). This is an approach-avoidance conflict; see section 3.4 for more details about the role of conflict in the BIS. Approach-avoidance conflicts were the most prominent conflict types described by participants (study 1). These conflicts lead to risk assessment behaviour to make sure that nobody notices hair loss or the actual behaviour of hair pulling, see figure 10.5 for details.

Participants described experiences of depression and anxiety in TTM, with depression being more problematic for them (study 1). This description reflects previous research (Grant et al., 2017) and our quantitative results in which only depression not anxiety contributed to prediction of those with TTM (study 3). According to our findings and r-RST, depression is experienced when the punishing stimuli is unavoidable, such as engaging in hair pulling after all effort to resist the urge is spent, as described within the theme ‘ego depletion’. Recalling that the function of the BIS is to increase arousal until a decision is made to approach or avoid a stimulus (3.2 and 4.5), it could be argued based on the included research that BIS involvement is implicated in TTM via goal conflict, and functions to increase avoidance behaviours.
### Constraint

**Ego depletion.** After long periods of attempting to resist the urge to pull, participants (69%) described feeling tired and exhausted due to being worn down by the urge until they no longer had energy to resist or fight it.

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### Emotion/state/cognition

#### Emotion/state/cognition (study 1)

**Depression and rumination.** While all participants had some experience with depression, the relationship between depression and hair-pulling ranged greatly. Typically, participants ruminated about themselves, their hair, and their life, such as thinking of oneself as a failure for not stopping the pulling behaviour, going bald, and being unhappy with their lives.

**Anxiety and worry.** Eighty-seven percent of participants explained that pulling regulated their experience of anxiety, or described feeling anxious because of the consequences of hair-pulling. For example, they worried about whether bald spots were noticeable to others, what would happen if others discovered their “secret”, and what would happen in the future with hair-pulling.

#### Emotion (study 3)

Depression, not anxiety predicts clinical level TTM

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### Behaviour (study 1)

**Risk assessment behaviour.** Seventy-five percent of participants described being hyper-vigilant to identify threats in the environment. Examples included regularly checking and rearranging hair, not holding long conversations, avoiding eye contact to divert attention, carefully observing one’s environment for signs of negative social evaluation, and choosing seating based on the likelihood of someone else seeing their hair loss.

### Stimuli (study 1)

**Reward versus punishment.** The majority of participants (87%) described a reward versus punishment conflict associated with hair-pulling behaviour. The conflict could be between behaviours, emotions and cognitions, and applied to pulling out a single hair, a hair-pulling episode, or the everyday experiences of living with TTM.

*To pull versus not pulling.* Participants (81%) described oscillating between approaching pulling and avoiding pulling, both behaviourally (e.g., repeatedly putting on and taking off a hat) and psychologically (e.g., telling oneself not to pull but feeling unable to resist hair-pulling urges). This conflict was described as “fighting with oneself”, “battling the urge”, or making a decision about whether to submit or continue to resist the urge to pull.

*Intimacy versus keeping hair-pulling a secret.* Participants (31%) described situations in which their intimacy with others was hampered by the need to keep hair-pulling a secret. This conflict was not exclusive to, but commonly experienced in, romantic relationships.

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*Figure 10.6 Visual representation of the BIS in trichotillomania*
10.2 Broader implications of our findings

Current findings point to a more complex underlying drive to hair-pulling than simply measuring the magnitude of impulsivity in response to reward, and compulsive avoidance of punishment. That is, differing conclusions can be drawn depending on the level of enquiry and severity of hair pulling symptoms. Firstly, when thinking about our findings based on level of enquiry, neurobiological evidence demonstrated functional dysregulation of reward processing in those with clinical TTM. From this it could be extrapolated that trait sensitivity to reward in a clinical cohort would be disordered. This was not the case. In fact, it was a self-report measure of sensitivity to punishment that demonstrated an almost significant relationship with the neurobiological processing of reward. Interestingly, these differing conclusions are reflected in and support the detailed descriptions of reward and punishment in our qualitative study. Secondly, we can compare results across level of symptom severity; this is most strikingly demonstrated in study 3. Using self-report measures, both sensitivity to reward and sensitivity to punishment predicted sub-clinical hair pulling symptoms from healthy controls, yet, it was depression and sensitivity to punishment that predicted clinical level symptoms of TTM.

It could be argued that it is co-morbid depression in those with TTM that leads to high trait sensitivity to punishment. Our approach was to consider depression as a part of TTM, based on theory. Within r-RST, depression is a result of not being able to avoid punishing stimuli. By definition, TTM is the inability to avoid hair-pulling (1.1), which is an unavoidable approach to punishing stimuli (3.1 and 3.4). Based on r-RST, depression is an inevitable aspect of TTM that we considered to be an important surface expression of the personality trait sensitivity to punishment and unresolvable goal conflict. Another explanation of high trait sensitivity to punishment in TTM is a vicious cycle in which trait
sensitivity to punishment leads to increased perception of threat (FFFS), which in turn
increases response to threat (BIS) resulting in more TTM symptoms.

Increased hair loss would correlate with more frequent and intense hair pulling
episodes. That is, as hair-pulling behaviour increases so too does the frequency and intensity
of threatening stimuli, thereby increasing FFFS and BIS activation, and by extension,
sensitivity to punishment. This idea is congruent with, and what we would expect based on r-
RST. The number and strength of threatening stimuli and/or symptom severity may influence
the level of trait sensitivity to punishment; yet this hypothesis was not addressed within our
studies.

Studies herein focused more on compulsivity than impulsivity yet the prominence of
both punishment and reward are consistent with current conceptualisations of TTM along
both impulsivity and compulsivity spectrums (Flessner et al., 2012; Hollander et al., 2006).
Findings place TTM well within the overlap of impulsivity and compulsivity (Figure 1.2,
Robbins et al., 2012) and address the tension within this overlap by identifying that
behaviours in TTM may be driven from differing levels; impulsiveness in TTM being driven
from biological origins and compulsiveness from a psychological and social level. This
interpretation supports previous findings of reward processing abnormalities (White et al.,
2013), striatal structural abnormalities (Isobe et al., 2018) and personality traits in TTM
(Hagh-Shenas et al., 2004; Keuthen, Tung, Altenburger, et al., 2015).

The separation of impulsiveness as neurobiological and compulsiveness as
psychological in our findings lends support to the idea that TTM may be thought of as a
‘compulsive habit’ (1.10). That is, a behaviour that occurs initially in response to reward, but
is maintained by avoidance of punishment once the initial reinforcement wears off (Robbins
et al., 2012; Vaghi et al., 2018). Although, according to our qualitative results reward has not
worn off completely. Participants described rewarding stimuli as being closely associated to the actual behaviour of hair pulling, such as chewing a hair follicle, whereas descriptions of punishing stimuli could be more distal, such as social stigma. This description indicates the learning of and generalisation of punishing stimuli and compulsivity over time. Although, this remains speculative in the absence of a longitudinal study measuring the contribution of reward and punishment over time in TTM.

When our fMRI and systematic review findings (study 4 and 5) are considered within the ‘fronto-striatal loops’ proposed by Robbins et al., (2012, Figure 1.5), an emphasis towards impulsivity and addiction on the neuropsychological/biological level is suggested. Our findings implicate the cingulate, putamen and caudate, which according to Robbins et al., (2012) may underlie stop-signal inhibition. The Stop-Signal Task was the only replicated neuropsychological test to report significant findings in a TTM cohort in the systematic review, although there was some inconsistency. These findings support the notion that ‘motor impulsivity’ (Hampton, et al., 2017) in TTM may have a biological basis (Bohne et al., 2008; Fineberg et al., 2010; Keuthen et al., 2007). Given that our fMRI findings indicate abnormal processing in areas of the brain related to stimulus-action-dependant reward prediction and reward-prediction error, it would be reasonable to hypothesise that motor impulsivity in TTM is a symptom of these faulty reward processes.
In summary, the role of reward and punishment in TTM differs according to the level at which they are measured, such as the biological and personality trait level. It also differs across the level of symptom severity. While supporting the notion that TTM can be placed around the middle of an impulsivity/compulsivity spectrum, our results indicate that a single spectrum does not adequately capture the complexity upon close investigation of the role of reward and punishment. Findings indicate that the level of reward and punishment
experienced within TTM can be relative to each other and drive behaviour together by interacting across levels. The emergence of punishment driven compulsive habits from behaviours that initially began through positive reinforcement embody such an interaction.

10.3 Discussion and implications for clinical practice

Overall, our results indicate an abnormal response to, and experience of, reward and punishment that requires change for long term recovery of TTM. In TTM, when symptom severity meets the DSM criteria, the experience of reward is concentrated exclusively and intensely when actively engaging in hair-pulling; the experience of reward more generally across life is absent. In contrast, the experience of punishment is pervasive and profound. Based on the included research for clinical level symptom severity, the goals of therapy needs to be; on the psychological level, an increase in the experience of reward covering multiple areas of life and a reduction of the intensity of general trait sensitivity to punishment. On the biological and behavioural level, decrease in the heightened experience of reward during pulling episodes is needed. As our research demonstrates, multiple levels of dysfunction: executive, cognition and beliefs, emotions, behaviours, motivation and personality traits, and biological changes, are involved in TTM, it follows that treatment aimed at changing the underlying motivation in TTM integrates these levels.

All of the treatment recommendations proposed within studies 1, 2 and 3, address the psychologically based element identified within the current research. In brief, these recommendations were to challenge maladaptive cognition around hair and self-worth. The use of behavioural activation was suggested to increase pleasure/reward across life, reduce dependence on pulling and take the onus of resisting the urge to pull.
The use of exposure and response prevention techniques was suggested to reduce the use of avoidance, and not only address what is avoided such as social or non-social stimuli but also address avoidance on multiple levels e.g. cognitive and behavioural. Finally, for those experiencing clinical level TTM, a focus on reducing passive avoidance, and minimising behavioural and cognitive response to threat is needed to address trait sensitivity to punishment. Once symptoms no longer meet clinical levels, an equal focus on response to reward and punishment is recommended. These treatment recommendations can be implemented within CBT.

A second treatment element aimed at rectifying reward-processing dysfunction is needed. With an underlying biological dysfunction in reward processing specifically effecting brain areas responsible for stimulus-action-dependant reward prediction and reward prediction error (study 5), a more aggressive treatment than talk therapy and the standard HRT or CBT seems necessary for long term change. This is evidenced by only the short term effectiveness of talk therapies (Slikboer et al., 2017), the chronicity of TTM (1.3) and our fMRI findings. While far from a new idea (Bayer, 1972), unpopular, and ethically ambiguous, aversion therapy may be useful in TTM treatment by generalizing the tendency to avoid punishment in TTM to avoidance of hair pulling, i.e., positive punishment. A vibration, bell or mild electrical shock may be an adequate stimuli. Indeed, a case study has provided preliminary evidence for the long term efficacy of aversive therapy in TTM (Crawford, 1988), given the recalcitrant long term addictive element of TTM it may be worth consideration. Aversive therapy is currently used for conditioning in alcohol dependence (Miller & Wilbourne, 2002; Smith, Frawley, & Polisser, 1991), head banging (Salvy, Mulick, Butter, Bartlett, & Linscheid, 2004), bed wetting (Schulz-juergensen, Langguth, & Eggert, 2014), and self-injurious behaviours (Linscheid & Reichenbach, 2002) that have otherwise proved intractable.
Our fMRI study indicates that an intervention aimed at decreasing brain activation in the striatum (or the reward brain network that included the striatum) is needed to address the underlying reward processing dysregulation inherent in TTM. The chronic nature of TTM and short term therapeutic outcomes to date warrant consideration of brain stimulation techniques. For example, transcranial magnetic stimulation (TMS) could be adapted for TTM. It is a non-invasive technique successfully used for treatment of depression, pain, motor stroke, and schizophrenia (Gomes, Brasil-neto, Allam, & De Souza, 2012; Lefaucheur et al., 2014). Trials examining TMS for the treatment of OCD (the diagnostic condition with the most symptom overlap with TTM) have revealed mixed results. The dorsal lateral prefrontal cortex is the target of choice for OCD and depression. It is involved in numerous functions from executive processing to motor planning. Given the important role of stimulus-action-reward associations i.e., habit formation in TTM and the emphasis on motor patterns in TTM (study 4) it may be worthwhile investigating TMS applied to the motor cortex while an individual preforms hair-pulling motor patterns in an attempt to dissociate the reward-motor pattern association. Treatment would need to be conducted in a research setting as no trials of TMS in TTM have been identified in the literature. The type of TMS - repetitive or deep, dose and duration of treatment remains to be investigated.

Deep brain stimulation (DBS) involves invasive brain surgery, which may be a treatment option for the very worst cases. It has shown promise in OCD (Koning, Figee, & Denys, 2011), with striatal areas being targeted. The junction of the anterior capsule, anterior commissure and posterior ventral striatum has been found to be an ideal site of stimulation in OCD (Greenberg et al., 2008), this knowledge may guild electrode placement in TTM. Electrode placement may be crucial for the treatment of TTM with
DBS, as DBS has resulted in increased impulsive behaviours when used for treatment of Parkinson disease (Vloo, Raymaekers, Kuyck, & Nuttin, 2017). Whether a targeted brain structure is excited or inhibited may depend on the direction of messages (afferent or efferent), and the neurotransmitters of the stimulated region (Chiken & Nambu, 2016; Vitek, 2002). Based on our fMRI findings, an aim of DBS may be to inhibit the over-activated areas of the putamen, pallidum and caudate, by stimulating the inhibitory axons leading to those areas.

Also useful for the long-term reduction of symptoms may be a long-term structured social program, such as commonly used for other addictions, which could provide social support, accountability and motivation during and at completion of short-term treatments. Participants highlighted social and motivational issues as important to their experience of TTM in our qualitative study. A lack of active coping, as demonstrated by pervasive avoidance in the current research, could be addressed by such programs (Humphreys, Mankowski, Moos, & Finney, 1999; Longabaugh, Wirtz, Zweben, & Stout, 1998; Morgenstern, Labouvie, Mccrady, Kahler, & Prey, 1997). Group treatment programs have been trialled in TTM and these programs could be extended or include additional elements of social support, accountability and motivation (Diefenbach et al., 2006; Toledo et al., 2015).

The longer cognitive behaviour therapy program of 22 weeks (Toledo et al., 2015) versus the eight week behaviour program (Diefenbach et al., 2006), seemed to be more effective by the end of the program. Yet, in both studies, supportive therapy also provided a reduction in symptoms. A long-term integrated program of both 22 weeks of CBT and 22 weeks of supportive therapy or self-help, may contribute to long-term maintenance of treatment gains. Combining CBT with alternate sessions of supportive therapy (one-on-one or in a group) would reduce the financial cost of a longer-term
treatment. A more affordable health care professional than a psychologist can deliver supportive therapy. The longer-term treatments and support used to maintain abstinence in addiction might prove valuable in addressing the impulsive and rewarding element of TTM.

10.4 Implications for further research

More imaging and motor deficit studies are needed to clarify how reward motivated impulsive behaviour occurs in TTM; whether there is a relationship between reward processing and motor inhibition, and whether there is a relationship with sensitivity to reward and punishment personality traits and motor inhibition. The evidence presented does not reflect typical findings associated with reward-motivated addiction. Indeed, deficits of behaviour inhibition are only found applicable to some drug addictions (Smith, Mattick, Jamadar, & Iredale, 2014) and unlike neurocognitive testing in gambling disorder (Timmeren, Daams, Holst, & Goudriaan, 2018) our systematic review of neuropsychological research in TTM did not find convincing evidence of any deficits. Only one replication was found demonstrating impaired ability to suppress automatic motor reactions; the remaining evidence was mixed (study 4). Further, our fMRI findings do not agree with those associated with drug addiction, demonstrating increased activation of the ventral striatum (Luijten, Schellekens, Kuhn, Machielse, & Sescousse, 2017); or gambling addiction, demonstrating decreased activation of the dorsal striatum (Luijten et al., 2017).

We found abnormal activation of the dorsal striatum (putamen, palladium and caudate) in TTM; structural abnormalities are also reported in these brain regions (Isobe et al., 2018). These regions are responsible for habit learning, which occurs via synaptic plasticity; long-term potentiation strengthens a connection, and long-term depression weakens a
connection. Both processes are affected by the number of activated glutamate receptors, and level of glutamate in the synapse (Lovinger, 2010). Indeed, n-acetylcysteine, a glutamate precursor that reduces the synaptic release of glutamate, has demonstrated reductions of TTM symptoms (Grant et al., 2009). Of the currently trialled medications for TTM, the fMRI study points to n-acetyl cysteine as the most promising. A longitudinal fMRI study measuring the effect of n-acetyl cysteine on reward response in TTM may help elucidate mechanisms of neurological plasticity in the striatum needed for long term behaviour change.

Also, a within-groups study of resting state versus symptom provocation, in which those with TTM engage in hair pulling during scanning, may prove helpful in targeting brain areas for treatments. While such studies have been conducted in OCD e.g. (Adler et al., 2000), correlates between TTM symptoms and underlying functional brain regions remain theoretical. Such knowledge of TTM may open up future treatment options such as deep brain stimulation and transcranial magnetic stimulation that have already shown usefulness in OCD (Gomes et al., 2012; Vloo et al., 2017). Although, given the impulsive element already included in TTM, risk of new impulsive behaviours would need to be considered, such as when deep brain stimulation is used for Parkinson disease (Merola et al., 2017).

Current results indicate an element of both compulsive punishment avoidant behaviour and a narrow intensive experience of impulsive approach to reward in TTM. Within this program of research we have provided a statistical description of avoidance (study 2). An investigation of approach behaviours remains to be carried out. The current approach that uses phenomenological exploration using mixed methods approaches may be a useful starting point. Quantified descriptions of impulsive behaviour should further guide development of psychological treatments, as should delineation of motor impulsiveness and reward impulsiveness in a cohort of TTM.
Investigation of underlying biological measures of arousal in TTM, such as cortisol levels, could further elucidate underlying motivation. Defined cycles of biological arousal in those with TTM would also significantly increase the legitimacy of a number of TTM theories and strengthen arguments around the role of emotional triggers for hair-pulling behaviour. This could be explored using between group designs, comparing cortisol levels of TTM with healthy controls, gambling addiction or other addictions and OCD.

10.5 Methodological considerations
10.5.1 Limitations

No measures of impulsivity and compulsivity were used in this research, limiting their discussion. This was deliberate to maintain the focus of the research on motivation and behaviours defined within r-RST. Yet, the self-report measures chosen have resulted in ambiguity around theoretical interpretation. Both the SPSRQ (Torrubia et al., 2001) and BIS/BAS scales (Carver & White, 1994) were created based on the original RST, but results have been discussed and interpreted within the r-RST. While use of an updated scale reflecting the r-RST would have been ideal, the new scales tend to lack the validity and acceptance within RST research; the Jackson 5 scale (Jackson, 2009) reflecting the individual flight, fight and freeze systems is one example (Corr, 2016). Both the SPSRQ and BIS/BAS scales were adequate to address the core question of this research, as they both capture variations of response to reward and punishment that drive behaviour in the original and revised RST. Indeed, it has been argued that the BIS/BAS scales includes the FFFS, reflecting the revised theory (Heym et al., 2008).

A further limitation to the studies herein is the use of the MGH as a measure of TTM severity. The MGH has not been subjected to inter-cultural invariance testing, therefore, there
is the possibility of measurement error in our studies due to recruiting participants outside of the U.S. This is not the case for the BIS/BAS and SPSRQ scales, for which the psychometric properties have been tested and critiqued across cultures (Caci, Deschaux, & Bayle, 2007; Dufey, Fernandez, & Mourgues, 2011; Jorm et al., 1999; Torrubia et al., 2008).

While the between-group design of the included studies was necessary to detect ‘abnormal’ differences in response to reward and punishment, inherent in this design is the possible introduction of extraneous between-subjects variability. However, results across studies were consistent, or were explained by the use of different research methodology, indicating that extraneous variables did not overly influence conclusions. The inclusion of only women in studies 1 and 5 may have had some influence on results. While TTM is experienced by men, males were only included in the studies that collected data via the internet (studies 2 and 3). Specifically, this sex bias may have increased the importance of social elements of TTM in study 1 (Casati et al., 2000), and potentially inflated levels of depression (Kendler & Prescott, 1999).

10.5.2 Strengths

All studies within the thesis addressed the same question, which stemmed from the same theory, r-RST. What is the underlying motivation in TTM, attainment of reward or avoidance of punishment? The use of various research techniques - qualitative, statistical, literature synthesis and neuroimaging - produced a multi-layered and nuanced account of reward and punishment in TTM. Interpretation of results across such interdisciplinary studies resulted in unique insights into the drivers of hair-pulling behaviour. Across our studies, varying degrees of participant influence were facilitated, eliciting both subjective and objective results. Participants exercised a large influence on results in study 1, wherein they answered questions as they pleased. Participants had partial influence on results in the studies using questionnaires; researchers chose the questionnaires and participants were limited in
response format. At the objective extreme, participants had no influence on results in study 5, because the blood oxygen saturation level in fMRI operates outside of conscious awareness.

A further strength of our series of studies is the range of symptom severity included; healthy controls, sub-clinical hair-pulling and clinical level TTM. Inclusion of these three groups facilitated measurement and interpretation of underlying motivation at various symptom severity, and as such, demonstrates how motivation changes with severity. Study 3 embodied this approach, with a series of three studies exploring motivation across symptom severity levels, with the same self-report measures specifically designed to reflect RST.

With the exception of study 5, the sample sizes in the current work are not major limitations. Sample size prevented the use of advanced complex analyses such as multiple level MANOVA analyses in chapter 5, (n=573 and n=300), yet within this area of research these numbers are quite large. To the researchers knowledge we conducted the largest fMRI study worldwide to date and it was the first imaging study of TTM in Australia. Indeed, the large number of participants recruited for study 5 allowed for the exclusion of some participants data facilitating increased data quality. This rigour built on what was already a reliable and commonly used gambling task used for reward processing research (Delgado et al., 2003, 2000; Lutz & Widmer, 2014).

Further, the large sample size included in the qualitative analysis of study 1 (n=16) is far in excess of what is usual in qualitative research approaches (n=5 to 10). Sample sizes in qualitative research are typically smaller than those in quantitative research. Typically, qualitative research is conducted for rich descriptive detail, and not for the testing of hypotheses analysis (Anderson, 2010; Braun & Clarke, 2006; Elliott et al., 1999). The cohorts from studies 1 and 5 represented a range of demographic groups, and were recruited nationally. Participants from study 5 travelled long distances to participate making this study
the first conducted based on a national sample. Finally, the inclusion criteria for all studies were designed with a balance of scientific rigour, applicability to the clinical population and practicality in mind. A cohort of individuals who meet the DSM criteria for TTM, and no other DSM criteria, would be less relevant to the clinical presentation of TTM.

10.6 Conclusions

The research herein explicates the magnitude of influence that reward and punishment have in driving behaviour in TTM. The results have been condensed and presented as the motivational model of TTM, summarising the previously under explored area of motivation. Results not only support the notion that impulsivity and compulsivity contribute to TTM, but also present evidence indicating that: compulsivity, driven by avoidance of punishment is a psychosocial manifestation; and impulsivity, driven by approach to reward, is a biological manifestation. Implications for treatment and future research have been discussed.
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APPENDIX A ethics 2015/013

APPENDIX B ethics 2014/145

APPENDIX C ethics 2017/069

APPENDIX D ethics 2015/275

APPENDIX E - MGH
The Massachusetts General Hospital (MGH) Hair Pulling Scale

APPENDIX F - SPSRQ
Sensitivity to Punishment and Sensitivity to Reward Questionnaire

APPENDIX G - BIS/BAS scales
BIS/BAS scales

APPENDIX H - SCS
Self-Concealment Scale

APPENDIX I - CBAS
Cognitive-Behavioral Avoidance Scale (CBAS)
21 APPENDIX J - AAQ

Acceptance and Action Questionnaire

22 APPENDIX K - DASS

Depression Anxiety and Stress Scale, short version

23 APPENDIX L – TIS/TSS

The NIMH Trichotillomania Scales
Trichotillomania Impairment Scale / Trichotillomania “Global” Scale

The NIMH Trichotillomania Scales
Trichotillomania Symptom Severity Scale (NIMH-TSS)

24 APPENDIX M – fMRI gambling task

Figure A1, A - gambling task used in our fMRI study, B – temporal and scanning sequence of events, figure taken from (Delgado et al., 2000).

25 APPENDIX N – Supplemental material study 1.

Qualitative Interview Guide
APPENDIX O - Supplemental material study 2.

Table A1. Factor Loadings of the Six-Factor Solution from the EFA

Table A2. Items of the Five Factor Model of Avoidance in Hair-pulling from the CFA

APPENDIX P – Supplemental material study 4
APPENDIX Q - Authorship indication form study 1

Swinburne Research
Authorship Indication Form
For PhD (including associated papers) candidates

NOTE
This Authorship Indication form is a statement detailing the percentage of the contribution of each author in each associated 'paper'. This form must be signed by each co-author and the Principal Coordinating Supervisor. This form must be added to the publication of your final thesis as an appendix. Please fill out a separate form for each associated paper to be included in your thesis.

DECLARATION
We hereby declare our contribution to the publication of the 'paper' entitled:

Title: Research and punishment are viewed by individuals experiencing trichotillomania according to revised reinforcement sensitivity theory

First Author
Name: Lenaeta Shukbour Signature: 
Percentage of contribution: 80 % Date: 24/10/2017

Brief description of contribution to the 'paper' and your central responsibilities/role on project: Conducted all aspects of the study

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Brief description of your contribution to the 'paper': Contribution to analysis and manuscript

Third Author
Name: Luke Smith Signature: 
Percentage of contribution: 5 % Date: 11/12/17

Brief description of your contribution to the 'paper': Gave theoretical guidance and contributed to manuscript

Fourth Author
Name: Maja Nedeljkovic Signature: 
Percentage of contribution: 5 % Date: 26/10/2017

Brief description of your contribution to the 'paper': Overall supervision and contribution to manuscript

Principal Coordinating Supervisor: Name: Maja Nedeljkovic Signature: 
Date: ___/___/____

In the case of more than four authors please attach another sheet with the names, signatures and contribution of the authors.
NOTE
This Authorship Indication form is a statement detailing the percentage of the contribution of each author in each associated 'paper'. This form must be signed by each co-author and the Principal Coordinating Supervisor. This form must be added to the publication of your final thesis as an appendix. Please fill out a separate form for each associated paper to be included in your thesis.

DECLARATION
We hereby declare our contribution to the publication of the 'paper' entitled:

First Author
Name: Susan Russell  Signature: 
Percentage of contribution: 5%  Date: 26/10/13
Brief description of contribution to the 'paper' and your central responsibilities/role on project: Contribution to manuscript

Second Author
Name: ___________________________  Signature: ___________________________
Percentage of contribution: ___%  Date: __/__/____
Brief description of your contribution to the 'paper':

Third Author
Name: ___________________________  Signature: ___________________________
Percentage of contribution: ___%  Date: __/__/____
Brief description of your contribution to the 'paper':

Fourth Author
Name: ___________________________  Signature: ___________________________
Percentage of contribution: ___%  Date: __/__/____
Brief description of your contribution to the 'paper':

Principal Coordinating Supervisor: Name: ___________________________  Signature: ___________________________
Date: __/__/____

In the case of more than four authors please attach another sheet with the names, signatures and contribution of the authors.
29 APPENDIX R - Authorship indication form study 2

Swinburne Research

Authorship Indication Form
For PhD (including associated papers) candidates

NOTE
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DECLARATION
We hereby declare our contribution to the publication of the 'paper' entitled:

First Author
Name: Renata Shklover Signature: [Signature]
Percentage of contribution: 30.8 % Date: 12/12/12
Brief description of contribution to the 'paper' and your central responsibilities for the project:

Second Author
Name: David Clarke Signature: [Signature]
Percentage of contribution: 5 % Date: 3/12/12
Brief description of your contribution to the 'paper': Comments on manuscript, supervision

Third Author
Name: Maja Nedeljkovic Signature: [Signature]
Percentage of contribution: 5 % Date: 26/12/12
Brief description of your contribution to the 'paper': Comments on manuscript, supervision

Fourth Author
Name: Simon Rosselll Signature: [Signature]
Percentage of contribution: 5 % Date: 26/12/12
Brief description of your contribution to the 'paper': Comments on manuscript, supervision

Principal Coordinating Supervisor: Name: Maja Nedeljkovic Signature: [Signature]
Date: [Date]

In the case of more than four authors please attach another sheet with the names, signatures and contribution of the authors.
APPENDIX S - Authorship indication form study 3

Swinburne Research

Authorship Indication Form
For PhD (including associated papers) candidates

NOTE
This Authorship Indication form is a statement detailing the percentage of the contribution of each author in each associated ‘paper’. This form must be signed by each co-author and the Principal Coordinating Supervisor. This form must be added to the publication of your final thesis as an appendix. Please fill out a separate form for each associated paper to be included in your thesis.

DECLARATION
We hereby declare our contribution to the publication of the ‘paper’ entitled:

Motivation underlyinghair-pulling behavior conceptualized by the reinforcement sensitivity theory of personality

First Author
Name: Renata Shkypec, Signature: 
Percentage of contribution: 25 %
Date: 2/12/2017
Brief description of contribution to the ‘paper’ and your central responsibilities/role on project: Participant recruitment, data collection, data analysis, design, wrote the first draft of the manuscript

Second Author
Name: Maya Nedeljkovic, Signature: 
Percentage of contribution: 5 %
Date: 6/12/2017
Brief description of your contribution to the ‘paper’: Comments on manuscript and supervision

Third Author
Name: David (first) Signature: 
Percentage of contribution: 5 %
Date: 13/12/2017
Brief description of your contribution to the ‘paper’: Comments on manuscript and supervision

Fourth Author
Name: Susan Russell, Signature: 
Percentage of contribution: 5 %
Date: 26/12/2017
Brief description of your contribution to the ‘paper’: Comments on manuscript and supervision

Principal Coordinating Supervisor: Name: Maya Nedeljkovic, Signature: 
Date: 26/12/2017

In the case of more than four authors please attach another sheet with the names, signatures and contribution of the authors.
This Authorship Indication form is a statement detailing the percentage of the contribution of each author in each associated paper. This form must be signed by each co-author and the Principal Coordinating Supervisor. This form must be added to the publication of your final thesis as an appendix. Please fill out a separate form for each associated paper to be included in your thesis.

We hereby declare our contribution to the publication of the 'paper' entitled:

**A systematic review of published primary studies of neuropsychology and neuroimaging in schizophrenia**

First Author

Name: **Annika Silver**
Signature: [Signature]

Percentage of contribution: 90%
Date: 26/7/2017

Brief description of contribution to the 'paper' and your central responsibilities/role on project: Conducted systematic review, design, data synthesis, wrote first draft of the manuscript.

Second Author

Name: **Maree Reser**
Signature: [Signature]

Percentage of contribution: 5%
Date: 5/12/2017

Brief description of your contribution to the 'paper': Contributed to screening included studies.

Third Author

Name: **Maja Nedeljkovic**
Signature: [Signature]

Percentage of contribution: 5%
Date: 26/1/2017

Brief description of your contribution to the 'paper': Comments on manuscript and supervision.

Fourth Author

Name: **David Castles**
Signature: [Signature]

Percentage of contribution: 5%
Date: 13/12/17

Brief description of your contribution to the 'paper': Comments on manuscript and supervision.

Principal Coordinating Supervisor: Name: **Dr Maja Nedeljkovic**
Signature: [Signature]
Date: [Date]

In the case of more than four authors please attach another sheet with the names, signatures and contribution of the authors.
Swinburne Research

Authorship Indication Form
For PhD (including associated papers) candidates

NOTE
This Authorship Indication form is a statement detailing the percentage of the contribution of each author in each associated 'paper'. This form must be signed by each co-author and the Principal Coordinating Supervisor. This form must be added to the publication of your final thesis as an appendix. Please fill out a separate form for each associated paper to be included in your thesis.

DECLARATION
We hereby declare our contribution to the publication of the 'paper' entitled:

A systematic review of published anatomy studies of neuropsychology and neuroimaging in schizophrenia

First Author
Name: Svena Rossell
Signature: [Signature]
Percentage of contribution: 5%
Date: 26/10/13
Brief description of contribution to the paper and your central responsibilities on project: Comments on manuscript and supervision

Second Author
Name: 
Signature: 
Percentage of contribution: ____%
Date: _/_/____
Brief description of your contribution to the paper:

Third Author
Name: 
Signature: 
Percentage of contribution: ____%
Date: _/_/____
Brief description of your contribution to the paper:

Fourth Author
Name: 
Signature: 
Percentage of contribution: ____%
Date: _/_/____
Brief description of your contribution to the paper:

Principal Coordinating Supervisor: Name: 
Signature: 
Date: _/_/____

In the case of more than four authors please attach another sheet with the names, signatures and contribution of the authors.
APPENDIX U - Authorship indication form study 5

Swinburne Research

Authorship Indication Form
For PhD (including associated papers) candidates

NOTE

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DECLARATION

We hereby declare our contribution to the publication of the 'paper' entitled:

'Peer-led punishment in distilled: Managing fMRI versus self-report'

First Author
Name: Donela Slikhoer Signature: ________________
Percentage of contribution: 30.0 % Date: 14/12/2017
Brief description of contribution to the 'paper' and your central responsibilities/role on project:
Conducted all aspects of the research except fMRI analysis

Second Author
Name: Matthew Hughes Signature: ________________
Percentage of contribution: 6 % Date: 14/12/2017
Brief description of your contribution to the 'paper':
FMR analysis and manuscript

Third Author
Name: Maya Nedeljkovic Signature: ________________
Percentage of contribution: 2 % Date: 14/12/2017
Brief description of your contribution to the 'paper':
Supervision and manuscript

Fourth Author
Name: David Castle Signature: ________________
Percentage of contribution: 2 % Date: 14/12/2017
Brief description of your contribution to the 'paper':
Supervision and manuscript

Principal Coordinating Supervisor: Name: ________________ Signature: ________________
Date: 14/12/2017

In the case of more than four authors please attach another sheet with the names, signatures and contribution of the authors.
Swinburne Research

Authorship Indication Form
For PhD (including associated papers) candidates

NOTE

This Authorship Indication form is a statement detailing the percentage of the contribution of each author in each associated ‘paper’. This form must be signed by each co-author and the Principal Coordinating Supervisor. This form must be added to the publication of your final thesis as an appendix. Please fill out a separate form for each associated paper to be included in your thesis.

DECLARATION

We hereby declare our contribution to the publication of the ‘paper’ entitled:

Last Author

Name: ___________ Signature: ____________________________

Percentage of contribution: ___% Date: __/__/____

Brief description of contribution to the ‘paper’ and your central responsibilities/role on project:

Second Author

Name: ______________________________ Signature: __________________________

Percentage of contribution: ___% Date: __/__/____

Brief description of your contribution to the ‘paper’:

Third Author

Name: ______________________________ Signature: __________________________

Percentage of contribution: ___% Date: __/__/____

Brief description of your contribution to the ‘paper’:

Fourth Author

Name: ______________________________ Signature: __________________________

Percentage of contribution: ___% Date: __/__/____

Brief description of your contribution to the ‘paper’:

Principal Coordinating Supervisor: Name: __________________________ Signature: __________________________

Date: __/__/____

In the case of more than four authors please attach another sheet with the names, signatures and contribution of the authors.
33  APPENDIX V – Copyright agreement, Study 1
34  APPENDIX W – Copyright agreement, Study 2
APPENDIX X – Copyright agreement, study 4