UNIVERSITY OF TURKU

Brain White Matter Abnormalities in Binge Eating Disorder

Human Neuroscience / Faculty of Medical Science

Master's thesis

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Subject: Human Neuroscience
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Title: White Matter Alterations in Binge Eating Disorder
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Number of pages: 58
Date: 28/01/2026

Binge eating disorder (BED) is characterised by loss of control around feeding behaviour. Patients suffer from binge eating episodes, where they consume large amounts of food even to a point of feeling uncomfortable fullness. An important clinical difference between binge eating disorder and bulimia nervosa, is that in binge eating disorder, patients do not use compensatory mechanisms, such as self-induced vomiting or over-exercise. It is a disorder that is associated with significant clinical impairment, but its neurobiological underpinnings remain poorly understood.

In this pilot study, diffusion tensor imaging was used to examine white matter organisation in patients with a binge eating disorder by comparing diffusion imaging measures across patients with a binge eating disorder, gambling disorders, and healthy controls. Gambling disorder was chosen as a comparison group as binge eating disorder shares many clinical and symptomatic similarities behavioural addictions. Gambling disorder is currently the only officially recognised behavioural addiction.

Diffusion tensor imaging data were analysed to assess fractional anisotropy, mean diffusivity, axial diffusivity, and radial diffusivity. Group comparisons were conducted to identify differences in white matter microstructure and clinical and demographic variables, including symptom severity scores and body mass index.

Individuals with BED exhibited significantly higher fractional anisotropy across multiple right-hemispheric white matter regions compared to both healthy controls and the gambling disorder group. BED exhibited increased FA in the retro lenticular part of the internal capsule and the posterior corona radiata compared to the healthy control group. Compared to the gambling group, BED group had increased FA in the anterior, superior, and posterior corona radiata, the body of corpus callosum, the posterior thalamic radiation, and the retro lenticular part of internal capsule. No significant differences in other diffusion measures were observed. Additionally, elevated FA positively correlated with binge eating severity and negatively associated with body mass index.

These findings offer an insight into the neurobiology of binge eating disorder and suggest that BED may be associated by altered brain white matter organisation that differs from gambling disorder. Elevated FA in the absence of changes in other diffusion measures may reflect abnormalities in network organisation or there may be constrained efficiency, rather than pure damage to white matter tracts that is typically associated with reduced FA.

Key words: Binge eating disorder, Addiction, Behavioural addiction, White matter, White matter tracts, Diffusion tensor imaging, Eating disorder.

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1 Introduction

Eating disorders are amongst some of the most severe type of psychiatric illnesses as they exhibit high rates of mortality, comorbidities, such as anxiety and depression, as well as impairment in functioning. The lifetime prevalence of all eating disorders taken together is 2-5% in many populations. The medical, psychological, and social burden of eating disorders are significant (Attia & Walsh, 2025; Hambleton et al., 2022). Eating disorders involve disturbance in eating behaviour, as well as emotional dysregulation around food intake (Bohon, 2019). The symptoms of Binge Eating Disorder (BED), which is one of the most common type of eating disorders worldwide, include episodes of excessive food consumption, which is accompanied by a subjective sense of loss of control (Giel et al., 2022). BED shares some clinical similarities with Bulimia Nervosa (BN), as BN is another eating disorder characterised by binge episodes. However, individuals with BED do not exhibit compensatory mechanisms after binge episodes, such as self-induced vomiting or over-exercise, which are important clinical characteristics of BN (Dingemans et al., 2002). Even though BED is a clinically significant and prevalent disorder, it is currently severely under-researched particularly regarding its neurological underpinnings.

Over the past few decades, advances in neuroimaging have enabled researchers to explore the brain mechanisms underlying eating behaviours. This offers insight into how alterations in neural circuits contribute to disruptions in eating behaviours (Chen et al., 2024). BED in particular seems to involve functional dysfunctions in brain regions associated with reward processing, emotional regulation, and impulse control (Murray et al., 2023). Crucial brain areas involved are the striatum, prefrontal cortex, insula, and amygdala (Pasquale et al., 2024). However, functional differences alone may not fully capture the neural mechanisms underlying BED. Examining the brains' white matter architecture provides complementary insight into the structural pathways that support communication between distributed neural systems.

White matter integrity indicates the organisation and myelination of axonal fibres that connect different cortical and subcortical regions. White matter integrity is often affected in psychiatric conditions, as disruption in white matter structure can lead to impaired information transfer and dysregulation of network communication, which are processes that play a role in most psychiatric conditions, including depression, anxiety, schizophrenia, and bipolar disorder, for example (De Witte & Mueller, 2017; Koshiyama et al., 2020) . In the

context of BED, researching the integrity of white matter may help shed light to whether alteration in structural connectivity underlie the impaired feeding behaviour observed in this disorder.

The aim of this present study is to examine white matter integrity in individuals with BED, using diffusion tensor imaging (DTI). Specifically, this work seeks to identify white matter alterations in BED relative to healthy control, as well as compare alteration to those observed in Gambling Disorder (GD), which is a behavioural addiction that shares some clinical similarities with BED, such as problems with impulse control and a sense of loss of control over own behaviour. Furthermore, it aims to explore associations between white matter integrity and clinical characteristics, such as impulsivity and binge frequency. By investigating white matter changes in BED, this thesis aims to advance our understanding of how disruptions in structural connectivity contribute to the neurobiological mechanisms underlying maladaptive eating behaviours.

1.1 Binge eating disorder

1.1.1 Clinical and Epidemiological Overview of BED

1.1.1.1 Definition and diagnostic features

BED, which was first described as “night eating syndrome” as early as in 1959 by (Stunkard, 1959) when he was researching eating patterns and obesity, is an eating disorder characterised by recurrent, uncontrollable episodes of excessive food intake (binge episodes) (American Psychiatric Association, 2022). The absence of compensation behaviour, such as use of laxatives, self-induced vomiting or excessive exercise, is an important characterisation in the diagnosis of BED, and a crucial characteristic that separates it from other eating disorders, especially BN or Anorexia Nervosa Binge-Purging subtype (American Psychiatric Association, 2022; Keski-Rahkonen, 2021). During binge episodes, individuals experience a sense of loss of control, eat rapidly, and typically continue eating until feeling uncomfortably full. This is usually followed by feelings of guilt and shame (Bohon, 2019).

Although BED and recurrent binge eating episodes may naturally lead to weight gain and obesity, as binge episodes may lead to high calorific intake, BED is distinct from obesity, and obese people with or without BED have many behavioural, neurobiological, as well as genetic differences. Among those with BED who are also obese, the risk of medical complications

such as type 2 diabetes, mellitus, and hypertension are increased (Balodis et al., 2015; Davis, 2015). Among obese population, where BED is common, BED has estimated prevalence up to 30% in those who seek treatment for obesity (Estella et al., 2020; Giel et al., 2022; Kessler et al., 2016).

1.1.1.2 Epidemiology and Prevalence

Despite empiric studies suggesting that BED is one of the most common types of eating disorder worldwide, it is often not well recognised in healthcare, and many individuals never receive any treatment for it (Balodis et al., 2015; Keski-Rahkonen, 2021). The prevalence of BED has been estimated to be 1.5% of women and 0.3% of men worldwide. It is most prevalent in adolescence, but also often transient in nature (Keski-Rahkonen, 2021).

There is very limited data on the prevalence of BED in Finland, especially when it comes to the male population. However, according to twin studies, the lifetime prevalence of BED is around 0.7% in women in Finland, and 0.6% of adolescence women and 0.3% of adolescence men (Mustelin et al., 2015; Silén et al., 2020). Furthermore, in Finland, where ICD-10 is still in use, BED does not have its own diagnosis, and it is diagnosed as F50.8 “eating disorders not otherwise specified” (*muu syömishäiriö*). However, the World Health Organisation has already published ICD-11, where BED has its own diagnostic category, and it is slowly taken into use in Finland and other countries to improve recognition and diagnostic accuracy (WHO, 2024). Psychological distress, difficulties with self-acceptance, and shame surrounding symptoms often prevent individuals from seeking help from health care. Consequently, the true prevalence of BED may be higher than current estimates suggest (Keski-Rahkonen, 2021).

1.1.1.3 Course and Comorbidities

BED, like other eating disorders, often follows a chronic or recurrent course, with periods of remission and relapse. Although some studies show that up to half of patients may achieve at least some form of recovery or remission (Fairburn et al., 2000; Steinhaus and Weber, 2009), it is unclear how common complete and sustained recovery is. BED is associated with significant distress and impairments in performing daily tasks (functional impairments), as over 60% of individuals report some impairment and around 20% report severe impairment according to the Sheehan Disability scale, which measures how the disorder affects the

patients' daily life in terms of work or school, social life, and home or family responsibilities (Appolinario et al., 2022).

BED frequently co-occurs with many psychiatric disorders, such as major depressive disorder, anxiety disorders, attention deficit/hyperactivity disorder, and substance use disorders (Grilo et al., 2019). In addition to obesity and its linked effects, other medical comorbidities include metabolic syndrome, chronic pain, sleep disorders, and increased cardiovascular morbidity (Alagha et al., 2025; Hutson et al., 2018). These comorbidities contribute to increased healthcare utilization and poorer quality of life. Eating disorders, including BED, have the highest mortality rates of all psychiatric disorder (Val-Laillet et al., 2015).

1.1.1.4 Clinical Challenges and Treatment Approaches

In many cases with BED, there is often a cycle of trying to restrict or lose weight, often through extreme measures. The patients then experience a loss control, which leads to binging. Binging causes shame, which can then again lead to restriction, creating a vicious cycle. This is also why the main first step of treatment is to try and stop all weight loss attempts, especially through restrictive eating. It is also important for patients to aim for sufficient and regular meals, consumed every 3-4 hours (Elran-Barak et al., 2015).

Treatment methods for BED include psychiatric as well as medical intervention and treatment. Pharmacological treatments are typically used as an adjunct to psychotherapy. Selective serotonin reuptake inhibitors, especially fluoxetine/seronil at higher doses (60 mg/day), can reduce binge frequency and are particularly helpful for patients with comorbid depression (Costandache et al., 2023). Other pharmacological treatments include Lisdexamfetamine, which is currently the only FDA-approved medication for moderate to severe BED. It has been shown to reduce binge eating episodes and relapse risk (Costa et al., 2025). However, medications can also induce unpleasant side effects, such as insomnia, headache, and dry mouth (Costa et al., 2025; Heo & Duggan, 2017; Schneider et al., 2021). Some medications, including Lisdexamfetamine, might also have abuse potential, which has to be taken into consideration when considering treatment options (Richards et al., 2023). Other potential medications include topiramate, which is an antiepileptic agent associated with appetite suppression, and semaglutide, which is a GLP-1 receptor agonist that may reduce binge eating by modulating satiety and food reward signalling, though it is not yet approved for BED and long-term efficacy remains uncertain (McElroy et al., 2007; Nourredine et al., 2021; Richards et al., 2023).

Psychological interventions remain central to BED treatment. It seems, that the most effective psychological intervention is cognitive-behavioural therapy (CBT). It targets maladaptive cognitions around food, body image, and control. CBT has shown to significantly reduce binge frequency and improve emotional regulation. Both therapist-led CBT and guided self-help CBT formats seem to be effective. Family-based therapy is often recommended for children and adolescents, as the role of family in recovery and treatment at that age period is crucial. For BED patients, the key behavioural target in treatment is the establishment of structured, regular eating patterns (typically every 3-4 hours) and the cessation of restrictive dieting, as dieting often exacerbates binge-eating cycles (Keski-Rahkonen, 2021).

Although recovery is possible, relapse is common, and long-term remission rates remain modest. Current evidence suggests that combining psychological and pharmacological treatment yields the most promising outcomes (Hay, Philippa, 2023). Despite these interventions, many individuals continue to experience persistent symptoms, indicating that current approaches may not fully address the underlying neurobiological mechanisms (Hilbert et al., 2020).

Given its high prevalence, substantial psychiatric and medical comorbidities, as well as it often chronic course, BED represents a significant public health concern. That is why a deeper understanding of its neurobiological mechanisms may help inform more targeted and effective treatment in the future.

1.2 Neurobiology of BED

Although studies on the neurobiology of BED are still relatively limited, evidence increasingly supports the view that BED is characterised by dysregulation across interconnected neural systems that are associated with reward, motivation, emotion regulation, and cognitive control. It seems that individuals with BED exhibit an imbalance where subcortical reward and motivational circuits are overactive, while prefrontal self-regulatory and cognitive control systems are less activated. Such imbalance may underlie the inability to resist food cues, despite negative consequences, and lead to over eating (Amianto et al., 2015; Davis, 2015).

Current studies seem to implicate that key brain areas involved in BED include, for example, the prefrontal cortex (PFC), the ventral and the dorsal striatum, anterior cingulate cortex (ACC), and amygdala (see Figure 1). In terms of BED, these brain areas and dysregulation

between these systems are associated with the above mentioned key characteristics of BED: hyperactivation of subcortical reward and motivation systems, hypoactivation of cognitive control, and disruptions in emotion regulation, leading to problems in feeding behaviours and inability to resist food cues (Hartogsveld et al., 2022; Kessler et al., 2016).

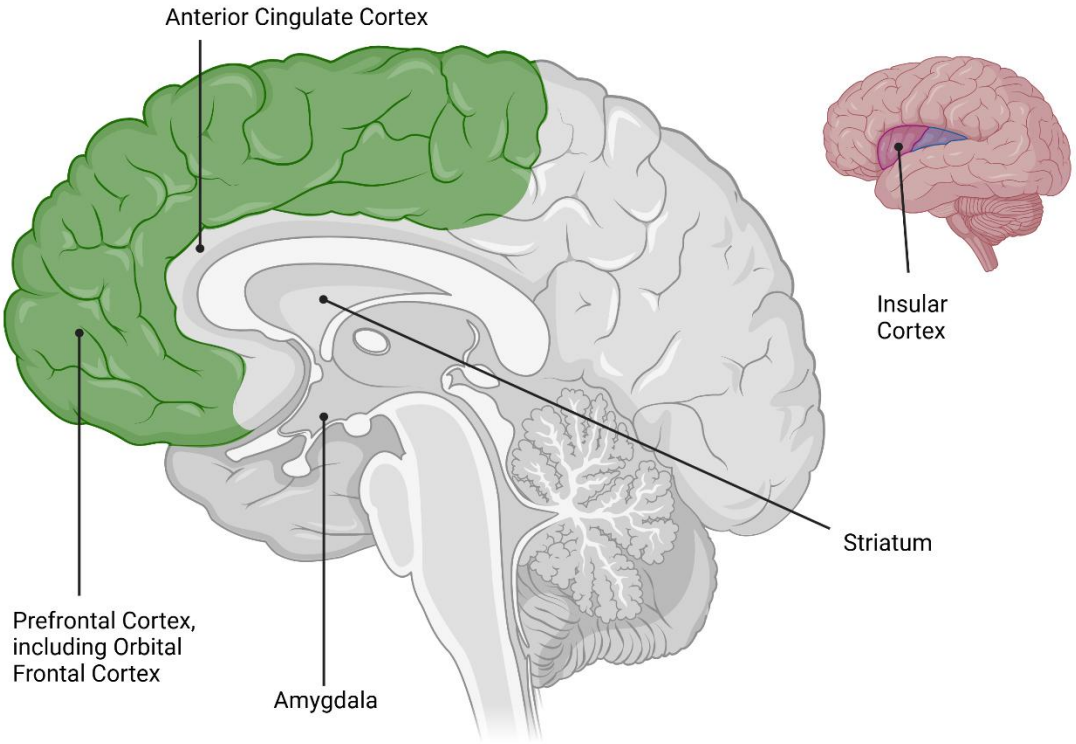

Figure 1: Schematic illustration of key brain regions implicated in binge eating disorder, including the prefrontal cortex (PFC), striatum, anterior cingulate cortex (ACC), and amygdala. These structures form interacting circuits involved in reward, cognitive control, and emotional regulation (Created in https://BioRender.com) (Adapted from a figure in a paper by (Kessler et al., 2016)).

1.2.1.1 Reward System Dysfunction

Overconsumption of high-fat and high-sugar foods in BED suggests that there might be alterations in reward processing and reward sensitivity. Many neuroimaging studies have examined food-cue reactivity, which refers to the neural responses when participants are exposed to palatable food stimuli (Balodis et al., 2015).

One of the earliest neuroimaging studies on the food-cue reward processing in BED population is a study by Geliebter et al., 2006. They used functional magnetic resonance imaging (fMRI) to study 20 participants, who were either lean or obese, and divided into

those with BED, and those without. When presented with visual and auditory stimuli of binge-type and non-binge-type foods, they found increased PFC activation in obese female participants with BED, whereas lean group with BED showed no such findings (Geliebter et al., 2006). This was one of the first studies to suggest that there could be differences in disruptions in reward processing in BED depending on the stage of the illness (Balodis et al., 2015; Bodell & Racine, 2023).

Balodis et al., 2013 studied monetary reward processing in obese individuals with and without BED using the monetary incentive delay task. Studies on reward processing that do not specifically involve food related cues, may produce additional insight into the disruptions in reward processing BED. Balodis et al. (2013) found that there were decreases in activity in the ventral striatum in the BED group compared to the obese non-BED group, during anticipatory reward/loss processing. These kind of findings further support not only the distinction of BED as a separate disorder from pure obesity, but also endorses that individuals with BED may process reward differently from other populations (Balodis et al., 2015; Balodis et al., 2013).

At neurochemical level, there is evidence that dopamine has an important role in this dysregulation of reward processing. In addictive paradigms, dopamine pathways mediate reward prediction errors and the learning of cue-reward associations. In BED, it seems that chronic over-exposure to palatable foods increases this dopaminergic signalling, reinforcing cue-driven approach behaviour (Avena & Bocarsly, 2012; Kessler et al., 2016). However, even though binge eating itself seems to cause increased dopamine release, some studies in obesity and related fields have shown reduced D2 receptor availability (Wang et al., 2001). Similar findings of D2 receptor downregulation have been demonstrated in BED animal studies. Furthermore, there also seems to be an increase in D1 and D3 receptor binding, suggesting that binge eating may contribute to changes dopaminergic gene expression. Binge eating itself likely causes acute dopamine spikes during episodes. Overtime, this may contribute to D2 receptor downregulation, as well as broader dopaminergic remodelling (Avena & Bocarsly, 2012; Mercante et al., 2024).

Evidence from multiple studies show that reward processing is dysregulated in BED. Specifically, studies indicate that individuals with BED may have paradoxical pattern of reward processing, meaning anticipation of food is hyper-responsive. Meanwhile, there is hypo-responsivity to the consumption of food, leading to a cycle, where increased amounts of

food are needed to feel satisfaction or reward. It also seems that the specific alterations in reward processing depend on the stage of the illness, as well as the reward type (Bodell & Racine, 2023). Studies also indicate that the disruptions are particularly in the dopaminergic mesolimbic pathway involving the ventral tegmental area (VTA), nucleus accumbens, and orbitofrontal cortex. These regions are, for example, critical for encoding salience, anticipation, and motivational value of rewarding stimuli, including highly palatable foods, the main reward cues in BED (Balodis et al., 2015; Morales & Berridge, 2020; Yohn et al., 2019).

1.2.1.2 Cognitive Control and Inhibitory Function

Research seems to indicate that while reward circuits may drive the urge to binge, prefrontal cortical regions, which are important in impulse inhibition, consequence evaluation, and adaptive regulation, for example, are often structurally weakened or less engaged. This could suggest that these deficits in prefrontal regions are central to the loss of control in BED (Lavagnino et al., 2016; Svaldi et al., 2025).

Functional imaging studies that use tasks requiring inhibition, such as Go/No-Go or Stroop task, often show hypoactivation in some prefrontal regions, such as dorsolateral prefrontal cortex (dlPFC), ACC, and inferior frontal gurys during response inhibition (Balodis et al., 2013; Svaldi et al., 2025). This could suggest that those with BED may have diminished top-down control when confronted with food-related impulses, however, there is also conflicting research especially when it comes to children and adolescence with BED; Murray et al., (2024), found no differences in neural activity in inhibitory or reward control circuitry in children with BED compared to children without BED. In addition, Lock et al., (2011) found that adolescence that exhibited binge eating behaviour had hyperactivation, instead of hypoactivation in many brain areas during a response inhibition task. This could again suggest that the specific changes in brain activation in BED may depend on the stage of the illness (Bodell & Racine, 2023; Lock et al., 2011; Murray et al., 2024).

In addition to inhibition control, meta-analyses and some case-control studies report deficits in executive functions, such as set-shifting and working memory in individuals with BED (Cury et al., 2020; Duchesne et al., 2010), which is something that has also been reported in many other eating disorders, such as Anorexia Nervosa and BN (Diaz-Marsa et al., 2023). A meta-analysis Cury et al., (2020) found that individuals with BED exhibited poorer performance especially on working memory tasks compared to obese individuals without

BED, as well as poorer problem-solving performance. They, however, also point out that currently, although there is growing interest in the research of executive functioning in individuals with BED, many studies use varied methodology and small sample sizes, which may make it difficult to interpret results on a larger scale.

Delay discounting, which refers to preference for smaller immediate rewards over larger delayed ones, is another executive function where some studies have found that individuals with BED have alterations in performance (Manasse et al., 2015; McClelland et al., 2016). Specifically, many studies have observed that individuals with BED seem to prefer smaller, immediate rewards compared to larger, delayed ones (McClelland et al., 2016; Voon, 2015).

Connectivity studies also support the findings of weakened communication between control and reward regions. Frontostriatal tracts, which link PFC with basal ganglia networks, have shown altered connectivity in eating-disorder populations, suggesting that reward drives may more easily override regulatory input (Wierenga et al., 2014). It is possible that reduced connectivity between the dorsolateral PFC and striatum is associated with increased impulsivity, as well as poorer self-regulation, and increased craving for higher calorific foods (Haynos et al., 2021). Some researchers suggest that the weakened communication could lead to reward-driven impulses to more easily overdrive top-down regulatory input, which may contribute to binge episodes, as well as problems with delaying gratification (Balodis et al., 2015; McClelland et al., 2016).

1.2.1.3 Emotional and Interoceptive Processing

Beyond reward and control, emotion and interoceptive processing are essential for understanding BED. Some studies suggest that individuals with BED have difficulties with identifying, understanding, and regulating their emotions. The patients may also have problems with interpreting internal bodily cues, such as satiety and hunger, as well as emotional arousal. Brain areas that have been associated with the emotional and interoceptive processing in BED include the amygdala, which evaluates emotional salience and threat, and the insula, which integrates bodily signals, such as hunger, fullness, visceral states, with affective and motivational contexts (Craig, 2009; Poovey et al., 2022; Walenda et al., 2021). Patients with BED often also engage in maladaptive strategies to regulate their emotions, such as self-blame, rumination, and catastrophising (Walenda et al., 2021). Binge eating itself may be used as a method to obtain a momentary relief from negative emotions (Giel et al., 2022).

Neuroimaging studies in BED have reported heightened amygdala responsiveness to negative emotional stimuli and elevated insula activation when presented with food or interoceptive cues (Balodis et al., 2013; Celeghin et al., 2023). (Press et al., 2023) found that when presented with negatively valenced pictures of their own body parts, individuals with BED not only showed attentional bias towards these cues, but also higher activation in specifically the insula and amygdala when viewing these negatively valenced stimuli, but there were no differences in other brain areas, such as the ventromedial PFC or the fusiform body area, compared to control group. The authors suggest that individuals with BED may have processing bias towards body parts that they view negatively. These findings of increased amygdala and insula activation go together with the proposed model that emotional distress, as well as internal bodily states, such as discomfort or hunger, may be experienced more intensely by individuals with BED and drive the urge to binge (Balodis et al., 2015; Celeghin et al., 2023).

1.2.2 White and Gray Matter Alterations

Functional dysregulation is only part of the story; white matter architecture likely contains and shapes how these circuits interact, as white matter itself is important in connecting distributed brain circuits. White matter tracts facilitate efficient information transfer among neural regions. Altered white matter integrity may therefore underlie or exacerbate functional disconnection (Thiebaut de Schotten et al., 2020) In terms of reward processing, cognitive control, and emotional and interoceptive processing, functions affected in BED, white matter is crucial in integration of these processes, and disruptions may impair reward sensitivity, self-regulation, as well as emotional awareness (Bracht et al., 2015; Filley & Fields, 2016).

Estella et al. (2020), currently the only BED study using DTI, used tract-based spatial statistics (TBSS) to compare BED and control groups, finding increased fractional anisotropy (FA) in the forces minor, and increased axial diffusivity (AD) in the superior longitudinal fasciculus, cingulate gyrus, and corpus callosum. The researchers interpreted these alterations as markers of atypical white matter organization within networks linked to reward and cognitive control and may relate to impaired emotional regulation and decision-making in BED. However, whether these differences are predisposing traits, compensatory adaptations, or consequence of chronic binge eating remains unclear. Longitudinal and multimodal studies are needed to disentangle these possibilities.

Gray Matter (GM) alterations in BED involve brain areas particularly in reward processing, cognitive and impulse control, and appetite regulation. Interestingly, these changes have been observed in both paediatric and adult populations. Multiple studies have reported increased GM volume in the medial and lateral OFC, insula, ACC, and dorsolateral PFC compared to healthy controls and obese individuals without BED (Murray et al., 2022; Schäfer et al., 2010; Turan et al., 2021). These structural alterations could contribute to heightened reward sensitivity and impaired self-regulation, especially greater drive for food, observed in BED (Abdo et al., 2020; Schäfer et al., 2010).

1.2.3 Summary and Conceptual Frameworks

In summary, BED appears to be a disorder of dysregulated reward processing, impaired cognitive control, and emotional or interoceptive disruption, underpinned by functional hyperactivity in reward circuits and hypoactivity in regulatory circuits. However, the neurobiological basis of BED remains incompletely understood especially in terms of structural connectivity. Here lies the motivation for the present study: by analysing DTI data with TBSS, we aim to examine microstructural differences in white matter among individuals with BED, compared to those with GD, and healthy controls. Doing so may clarify whether BED shares connectivity patterns characteristic of behavioural addictions or reflects distinct neural signatures – ultimately advancing understanding of the disorder.

1.3 Shared neurobiological characteristics between BED and addictions

BED shares conceptual similarities with addictions that have led to proposal of an “addiction model of BED”. Addiction model of BED suggests that “food addiction” could be a high contributor to eating-related problems, and that foods that are high in sugar and fat may possibly trigger an addictive response in individuals with susceptible characteristics, such as impulsivity or dysfunction with reward processing (Schulte et al., 2016). High-fat and high-sugar foods may trigger the reward-related circuitry in similar manner as drugs of abuse (Gearhardt et al., 2011; Schulte et al., 2016). Still, “food addiction” and BED are, at least currently, seen as two different conditions or “food addiction” may be BED slightly reframed. Schulte et al., (2016) suggest that it may be more beneficial to try to examine the mechanisms underlying problematic eating behaviours to determine whether the conditions are addiction-like or whether an addictive process contributes to the disorder, than to try to differentiate between “food addiction” or BED conceptually.

GD is classified in the DSM-5 under Substance-Related and Addictive Disorders as the first recognised non-substance behavioural addiction (APA, 2013). It is characterised by persistent and recurrent maladaptive gambling behaviour that interferes with personal, social, and occupational functioning (Potenza, 2013; Chamberlain et al., 2018). GD is often associated with elevated impulsivity, poor decision making, and strong cure-reactivity to gambling-related stimuli – features that closely mirror those observed in BED during food-cue exposure. In clinical research, GD may provide a particularly useful comparison model for BED, as it allows investigation of addiction-related neural mechanisms without the confounding effects of chronic substance exposure (Finerber et al., 2014).

BED and GD are both characterised by compulsive engagement in rewarding behaviours, loss of control, craving, and persistence despite adverse consequences (Davis, 2015; Potenza, 2013). While BED involves the overconsumption of food and GD the maladaptive pursuit of gambling, both disorders reflect dysregulation in brain systems mediating reward, control, and emotion, similar to those implicated in substance use disorders (SUDs) (Mestre-Bach et al., 2020). However, BED does not seem to exhibit withdrawal and tolerance, at least not in the same manner as behavioural or substance addictions do (Schulte et al., 2016).

Both BED and GD can be conceptualised within an impulsivity-compulsivity spectrum, characterised by elevated impulsivity and compulsivity. Impulsivity refers to the inability to delay gratification and tendency to act prematurely without adequate forethought, whereas compulsivity refers to habitual and repetitive behaviours that are driven by relief from negative emotional states (Lozano-Madrid et al., 2023; Mestre-Bach et al., 2020). Both disorders also display increased craving, as well as cure reactivity. Craving and cue reactivity refer to motivational and physiological responses to disorder-specific stimuli, such as food and gambling cues. These are underpinned by overlapping neural circuits for reward and motivation, including the insula, ACC, and ventral striatum (Morales & Berridge, 2020)

Dysregulation of the brains' reward system is witnessed in both GD and BED. Areas that in particular seem to be affected are the ventral striatum and PFC. These regions are involved in reward processing, motivation, and impulse control, for example. Both disorders also share deficits in decision-making, especially under ambiguity or risk, which could suggest shared neurocognitive mechanisms (Kessler et al., 2016; Mestre-Bach et al., 2020). Furthermore, elevated impulsivity and compulsivity are common in BED and GD, and are linked to dysfunctions in corticostriatal circuits (Kessler et al., 2016; Lozano-Madrid et al., 2023).

Functional neuroimaging studies have demonstrated abnormal activation in overlapping brain regions among individuals with BED and GD, including the striatum, OFC, and ACC. These regions are critical for reward valuation, cognitive control, and error monitoring (Freinhofer et al., 2024; Haynos et al., 2021; Limbrick-Oldfield et al., 2017). Both groups show enhanced cue-reactivity in response to disorder-specific stimuli (food or gambling images) and reduced activation during tasks requiring inhibitory control, paralleling findings from substance addiction research (Haynos et al., 2021).

In terms of structural brain differences, BED is associated with greater grey matter volume in the ACC and medical OFC, and smaller volumes in the ventral striatum and caudate, compared to healthy controls (Hartogsveld et al., 2022). GD has different and generally less pronounced grey matter changes. In GD, smaller grey matter volume is often reported in the PFC, as well as the ACC and thalamus (Bellmunt-Gil et al., 2024; Raimo et al., 2021). This could indicate differences in neurobiological differences between these disorders; however, studies are still limited.

In addition, recent structural and connectivity studies highlight the importance of white matter integrity for the efficient communication between these neural systems. White matter tracts connect the prefrontal cortex to subcortical regions and are crucial for regulating impulse behaviour. Alterations in white matter microstructure have been reported in both BED and GD (Bellmunt-Gil et al., 2024; Estella et al., 2020).

DTI studies in GD have provided evidence of widespread alterations in white matter structure. For example, (Joutsa et al., 2011) found decreased white matter integrity in multiple brain regions, including the corpus callosum, the cingulum, the superior longitudinal fascicle, the inferior fronto-occipital fascicle, the anterior limb of internal capsule, the anterior thalamic radiation, the inferior limb of internal capsule, the inferior longitudinal fascicle and the inferior fronto-occipital fascicle. They propose that GD is associated with lower white matter integrity in multiple brain white matter tracts.

Similarly, Chamberlain et al. (2018) reported reduced fractional anisotropy (FA) in the corpus callosum and superior longitudinal fasciculus, suggesting disorganised or damaged white matter tracts in individuals with GD. More recent connectome-level analyses have revealed reduced connectivity within and to the frontal lobes, alongside striatal network reorganisation and an overall increase in global brain connectivity (Schimdt et al., 2023). These alterations

could reflect neural adaptations associated with impaired cognitive control and heightened reward sensitivity.

In summary, BED and GD share some significant behavioural, neurofunctional, and structural features, including heightened reward drive, impaired inhibitory control, and altered connectivity within cortico-striatal limbic networks. The identification of theses common neurobiological substrates could support the conceptualisation of BED within an addiction framework, however, there are also many differences between the disorders. Importantly, while both disorders show functional and structural alterations, GD offers a unique opportunity to examine addiction-related brain mechanisms without the confounds of substance exposure. Understanding the shared and distinct neural features of BED and GD may help clarify the neurobiological underpinnings of compulsive behaviour across disorders and guide the development of more targeted treatment approaches.

1.4 White matter

White matter consists primarily of myelinated axons, which form tracts that connect different cortical and subcortical regions of the brain. These tracts facilitate the rapid and efficient transmission of neural signals between distributed brain networks, allowing for the integration of cognitive, emotional, and motor processes. The degree of white matter integrity reflects how effectively these networks communicate and coordinate activity (O'Donnell & Westing, 2011).

In terms of eating disorders, which BED is classified as, knowledge about white matter alterations come mainly from studies about restrictive eating disorders, primarily Anorexia Nervosa, with a fewer number of studies on BN. Findings from studies on BN consistently show similar alterations as in Anorexia Nervosa (Gaudio et al., 2019; Olivo et al., 2017). Restrictive eating disorders consistently show disruptions in white matter structures especially during acute phases of disorders. Commonly affected brain areas include the corpus callosum, corona radiata, fornix, and thalamic radiations (Meneguzzo et al., 2019; Olivo et al., 2017; Vogel et al., 2016). It has also been documented that changes in white matter partially or even fully normalise after weight recovery, again suggesting that there are changes in white matter might be state-dependent changes (Olivo et al., 2017; Schwanenflug et al., 2019; Vogel et al., 2016). However, subtle abnormalities may persist even after long-term recovery, especially in those with more severe illness history (Schwanenflug et al., 2019; Yau et al., 2013).

Alterations in white matter structure can disrupt inter-regional communication and have been increasingly implicated in various psychiatric and behavioural disorders, including substance use disorders, obsessive-compulsive disorder (OCD), attention-deficit/hyperactivity disorder (ADHD), and behavioural addictions such as GD (Chamberlain et al., 2018; Joutsa et al., 2011). These conditions often involve dysregulated reward processing, impaired cognitive control, and altered emotional regulation, processes that depend on the integrity of fronto-striatal and limbic white matter connections (Yu et al., 2025).

Given that BED similarly involves abnormalities in reward sensitivity, impulsivity, and emotional control, investigating white matter microstructure may provide crucial insights into its neurobiological underpinnings. Specifically, white matter integrity can be viewed as a neural substrate for dysconnectivity, offering a potential mechanistic insight into the functional disinhibition and compulsive behaviour characteristic of BED and related disorders.

1.4.1 DTI

DTI is a non-invasive magnetic resonance imaging (MRI) technique that allows for the in vivo examination of white matter microstructure by modelling the diffusion of water molecules within brain tissue (Basser & Perpaoli, 1996). In white matter, water diffusion is anisotropic meaning it occurs preferentially along the direction of axonal fibres due to the presence of myelin sheaths and cellular membranes. By measuring this directional diffusion, DTI provides quantitative indices that reflect various aspects of white matter integrity (Jindal et al., 2025).

The main DTI metrics include Fractional Anisotropy (FA), which reflect the degree of directionality of water diffusion and is considered a marker of overall white matter integrity. This means, that higher FA usually indicates more coherent and intact fibre organisation. Mean Diffusivity (MD) is the another commonly reported DTI metrics. It represents the overall magnitude of water diffusion, and it is sensitive to changes in tissue density and extracellular space. Other less commonly used DTI metrics are Axial Diffusivity (AD) and Radial Diffusivity (RD), which are less commonly reported. AD reflects diffusion along the primary axis of the fibre and may relate to axonal integrity. Radial diffusivity, however, reflects diffusion perpendicular to the primary fibre axis and may relate to myelin integrity. Typically, reduced FA indicates there may be less organisation or damage to fibres. Increased MD or RD are interpreted as indicators of microstructural disruption, such as demyelination,

axonal damage, or reduced fibre coherence. Reduced AD is typically witnessed when there is axonal injury or degeneration (Alexander et al., 2007).

DTI is typically based on a diffusion-weight spin-echo echo-planar imaging (EPI) sequence, which is modified to be sensitive to diffusion effects by applying diffusion gradients in multiple directions. This allows for the estimation of diffusion tensors at each voxel and subsequent reconstruction of the diffusion properties across the brain (O'Donnell & Westin, 2011).

Analytically, DTI data can be examined using several approaches. Commonly, these include Tract based spatial statistics (TBSS), which is a voxel-wise, whole-brain method that aligns FA images from multiple subjects onto a common skeleton representing the core of major white matter tracts. Another research method is Region-of-interest (ROI) analysis, which focuses on predefined tracts or brain regions. Tractography, which reconstructs specific white matter pathways to assess connections between regions, is also often used. Each approach offers unique advantages, but TBSS has become the standard in group-level comparisons because it minimises alignment error and allows for objective voxel-wise statistical analysis across the entire white matter skeleton (Bach et al., 2014; Bigham et al., 2020).

DTI has proven highly sensitive to microstructural alterations even in the absence of gross anatomical abnormalities, making it particularly valuable in studying psychiatric and behavioural disorders where subtle connectivity changes are expected (Shizukuishi et al., 2013). However, it is important to note that is also has some limitations. For example, DTI measures are not specific to a single biological process, and the method can be affected by crossing fibres and partial volume effects, which can complicate interpretation. Furthermore, changes cannot be defined to a single biological process. This is why the findings in DTI studies should be interpreted with caution (Pasternak et al., 2018),

Findings from DTI studies across addiction-related and impulse control disorders have consistently demonstrated alterations in white matter integrity within fronto-striatal, limbic, and interhemispheric tracts. Such alterations are thought to reflect disruptions in circuits mediating reward, inhibition, and emotional regulation. Given the behavioural and neurobiological overlap between BED and disorders such as GD and SUDs, examining white matter integrity in BED may help to clarify whether similar connectivity disturbances contribute to its pathophysiology.

1.5 Aims and Hypotheses

The aim of the present study was to investigate white matter microstructural integrity in individuals with BED using DTI and to analyse the DTI data using TBSS. Specifically, this work sought to identify alterations in white matter structure associated with BED and to determine whether these alterations resemble or differ from those observed in GD, which is a behavioural addiction that shares core neurobiological features with BED, including heightened reward sensitivity, impaired impulse control, and compulsive behavioural patterns.

In addition to comparing BED with GD and healthy controls, the study also aimed to explore associations between white matter integrity and clinical characteristics, such as impulsivity and binge frequency, in order to better understand the relationship between structural connectivity and symptom severity.

Aims:

1. To examine differences in white matter integrity between BED, GD, and healthy control, as well as other eating disorders.
2. To compare BED and GD groups to assess whether the structural connectivity alterations in BED resemble those seen in behavioural addiction.
3. To investigate associations between DTI-derived white matter metrics and clinical measures, such as impulsivity and binge eating frequency, within the BED group.

Hypotheses:

1. Individuals with BED will show altered white matter integrity compared to healthy control, particularly within fronto-limbic and temporoparietal pathways implicated in reward processing and cognitive control. BED might show similarities with those usually found in other eating disorders.
2. BED and GD will display partially overlapping patterns of white matter alteration, reflecting shared disruptions in circuits mediating reward and impulse regulation.
3. Within the BED group, higher clinical measures, such as higher impulsivity and greater binge frequency will be associated with greater alterations in white matter integrity, particularly in tracts connecting prefrontal and striatal regions.

2 Materials and Methods

2.1 Participants

This study included 39 participants (7 participants with BED, 17 controls, 15 patients with GD). The data was gathered as a part of a bigger study that analysed a variety of neurobiological features through multimodal imaging. Briefly, the imaging protocol included Positron Emission Tomography (PET) with two different radiotracers ([^{11}C]Carfentanil in the morning for μ-opioid receptor binding and [^{18}F]FDOPA in the afternoon for dopamine synthesis capacity), task- and resting-fMRI, and structural MRI for gray and white matter measurements.

Fulfilling the DSM-IV criteria for BED or GD was the main inclusion criteria for participants. The diagnosis was confirmed with a structured clinical interview. Initially, thirteen subjects were excluded due to scheduling problems, four because they did not meet the diagnostic criteria for GD or BED, three were excluded due to alcohol abuse, two due to DSM IV axis 1 psychiatric disorder, and six were excluded due to other reasons.

2.1.1 Clinical characteristics of patients

In addition to age, sex, and BMI, the clinical and behavioural characteristics included length, weight, smoking, gambling hours and euros per week, and problematic gambling years. Furthermore, the participants completed following questionnaires: Pathological Gambling DSM-IV scores (PG DSM-IV) to assess gambling behaviour based on DSM-IV diagnostic criteria, South Oaks Gambling Screen (SOGS) to screen for gambling problems and severity, Alcohol Use Disorders Identification test (AUDIT) to screen for harmful alcohol use, as well as dependence symptoms and related problems. Barratt Impulsiveness Scale scores (BIS-11) were used to measure personality or behavioural trait of attentional, motor, and non-planning impulsivity, Beck's Depression Inventory (BDI) to assess presence and severity of depressive symptoms. The Balanced Empathy Scale (BES) was used to evaluate cognitive empathy levels and affective empathy. The Dutch Eating Behaviour Questionnaire (DEBQ) to measure eating styles, in particular emotional eating, eating in response to food cues (external eating), and dieting tendencies (restrained eating), and Yale Food Addiction Scale questionnaire (YALE) to assess symptoms of food addiction based on substance dependence criteria, meaning, for example, loss of control, tolerance, withdrawal, and impairment. In addition, for

BED participants, binge eating periods per week and problematic binge eating years were recorded.

2.2 Image acquisition

Each participant also underwent a brain MRI with a PET-MRI scanner Philips Ingenuity (Philips Healthcare, Cleveland, OH, USA). A 34-channel receiving head coil and a sagittal 3DTI-weighted TFE sense pulse sequence (TR 8.1 ms, TE 3.7 ms, flip angle 7°, matrix 256 × 256, 176 slices) with an isotropic voxel were used to gather anatomical reference images.

2.3 Diffusion MRI pre-processing and analysis

This data was pre-processed using QSI-prep. First, tract-based spatial statistics was run to allow voxelwise comparison of white matter integrity across participants, then FSL randomise to find statistically significant clusters, where there were significant differences between groups in FA, MD, AD, or RD.

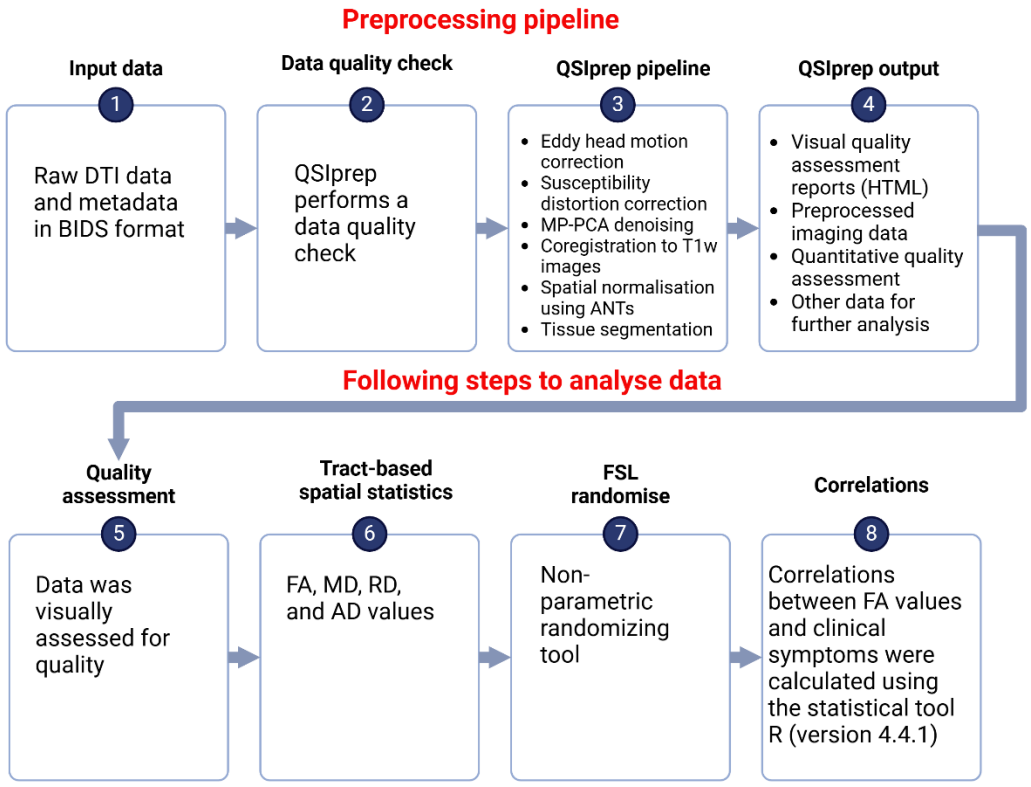

Figure 2: Preprocessing pipeline for the diffusion tensor imaging data (Created in https://BioRender.com). The input data in Brain Imaging Data Structure (BIDS) format was checked for quality. After this, the QSIprep pipeline was introduced, leading to the QSIprep output. Once the data

had gone through the QSIprep steps, the data was visually assessed for quality. After this, Tract Based Spatial Statistics (TBSS) and FSL randomise were performed. In addition, correlation calculations were done.

2.3.1 QSIprep preprocessing pipeline

QSIprep is an automated software tool used to preprocess diffusion MRI data. It uses standardised workflows to organise and process the data. This ensures consistency and reproducibility across subjects. QSIprep requires data to be organised in the Brain Imaging Data Structure (BIDS) format, which is a format commonly used in neuroimaging datasets. The software performs several preprocessing steps, including distortion and motion correction, it denoises the data and aligns the images to anatomical references (coregistration), and then resamples the scans into common space for further analysis (Figure x). As an output, it generates detailed visual reports and quality control metrics, which allow assessment of success and reliability of each preprocessing step.

After QSIprep performed the preprocessing pipeline, the data was visually inspected for any artefacts or abnormalities. Major artifacts were noticed in one of the control participants' B0 image. This participant was excluded from the study. The number of control participants in this study was 16 participants, 15 GD, and 7 BED.

Preprocessing was performed using QSIPrep 0.20.1.dev0+geda84d5.d20240112, which is based on Nipype 1.8.6 (Gorgolewski et al. (2011); Gorgolewski et al. (2018); RRID:SCR_002502).

2.3.1.1 Anatomical data preprocessing

Throughout the workflow, the T1-weighted (T1w) image, which was corrected for intensity non-uniformity using N4BiasFieldCorrection (Tustison et al. 2010, ANTs 2.4.3), was used as an anatomical reference. To reorient the anatomical reference image into AC-PC alignment, the 6-DOF transform extracted from a full Affine registration to the M NI152NLin2009cAsym template was used. Symmetric nonlinear registration via antsRegistration was then used to estimate a full nonlinear registration to the template from AC-PC space. To perform the brain extraction was on the T1w image, SynthStrip (Hoopes et al., 2022) was used. Automated segmentation was performed using SynthSeg (Greve et al., 2023) from FreeSurfer version 7.3.1.

2.3.1.2 Diffusion data preprocessing

All images with a b-value less than 100 s/mm^2 were considered as a b=0 image. MRtrix3's dwidenoise was used for the MP-PCA denoising (Veraart et al., 2016). MRtrix3's dwidenoise was applied with a 5-voxel window. After MP-PCA was performed on the data, the mean intensity of the DWI series was tuned. This was done so that all the mean intensity of the b=0 images matched across each individual DWI scanning sequence. After corrected images were resampled, B1 field inhomogeneity was corrected using dwibiascorrect from MRtrix3 with the N4 algorithm (Tustison et al., 2010).

To correct for head motion and Eddy current, FSL (version 6.0.5.1:57b01774)'s eddy was used (Andersson & Sotiropoulos, 2016). Eddy was arranged with a total of 5 iterations, q-space smoothing factor of 10, and 1000 voxels used to approximate hyperparameters. To characterise Eddye current-related spatial distortion, a linear first level model and a linear second level model were used. q-space coordinates were forcibly assigned to shells. It was attempted to distinguish the field offset from subject movement. After eddy, shells were aligned again. After this, Eddy's outlier replacement was run (Andersson et al., 2016). Data were then assigned in groups by slice. Only values from slices determined to contain at least 250 intracerebral voxels were included. If a group deviated by more than 4 standard deviations from the prediction, their data was replaced with imputed values. To perform the final interpolation, the Jac method was used.

Based on the preprocessed DWI, multiple confounding time-series were calculated, including framewise displacement. It was done with the implementation in Nipype, which works in accordance with the definitions by Power et al. 2014. The head-motion estimates, which were calculated in the correction step of the process, were placed within the matching confounds file. In addition, slicewise cross correlation was calculated. Furthermore, the DWI time-series were resampled to ACPC. This generated a preprocessed DWI, which was run in ACPC space with 1.7mm isotropic voxels. Nilearn 0.10.2 (Abraham et al., 2014) and Dipy (Garyfallidis et al., 2014) are used in multiple internal operations of QSIprep.

2.4 Tract-Based Spatial Statistics

Tract-Based Spatial Statistics (TBSS) is a tool used to analyse DTI data, specifically white matter integrity across subjects. It is applied to Fractional Anisotropy (FA), Mean Diffusivity (MD), Axial Diffusivity (AD), and Radial Diffusivity maps. TBSS projects each subject's

diffusion data onto a groupwise “skeleton” of major white matter tracts, which ensures that comparisons are made in corresponding anatomical locations.

The first step in TBSS involves generating FA maps from the preprocessed diffusion data. In this analysis, all DTI measure (FA, MD, RD, and AD) were investigated. These FA maps were created using the brain mask generated by QSIprep, together with corrected b-values**,** corrected b-vectors**,** and pre-processed T1-weighted images. This ensured consistent and accurate inputs for deriving the diffusion metrics required for TBSS.

Diffusion tensor fitting was performed using FSL (FMRIB Software Library). The command *dtifit* was applied to the pre-processed diffusion-weighted images (DWI) to generate diffusion metrics, including fractional anisotropy (FA), mean diffusivity (MD), as well as the three eigenvalues (L1, L2, L3) and three eigenvectors (V1, V2, V3). From these, axial diffusivity (AD) was defined as L1, and radial diffusivity (RD) was calculated as the mean of L2 and L3.

Tract-Based Spatial Statistics (TBSS) was then carried out using the standard FSL pipeline, consisting of the following steps:

- Preprocessing (tbss_1_preproc): FA images were resampled to a standard resolution.
- Registration (tbss_2_reg): Each subject’s FA image was nonlinearly registered to the FMRIB58_FA template in MNI152 standard space.
- Post-registration (tbss_3_postreg): A mean FA image was generated and thinned to produce a mean FA skeleton representing the centres of major white matter tracts common to the group.
- Projection (tbss_4_prestats): Each subject’s FA image was projected onto the mean FA skeleton.

The same nonlinear transformations and projection steps were applied to the MD, AD, and RD maps to enable voxel wise comparison of all diffusion-derived measures within the same white matter skeleton. Finally, voxel wise statistical analyses were performed on the skeletonized data using FSL Randomise with nonparametric permutation testing.

2.5 Statistical analysis

2.5.1 FSL Randomise

Voxelwise statistical analyses of the skeletonized diffusion metrics were performed using FSL Randomise, which implements non-parametric permutation testing. Design matrices and contrast files were constructed to specify pairwise group comparisons in both directions. Age, sex, and body mass index (BMI) were included as covariates to control for potential confounding effects on white matter microstructure, as previous studies have reported associations between BMI and white matter integrity. Statistical significance was assessed at $p < 0.05$, corrected for multiple comparisons, using 1,000 permutations. Threshold-Free Cluster Enhancement (TFCE) was applied to improve cluster sensitivity without the need for arbitrary thresholding. Significant clusters were identified and extracted using FSL's cluster command, and anatomical locations were labelled using FSLeyes with the JHU ICBM-DTI-81 White-Matter Labels Atlas.

2.5.2 Statistical Correlations

Correlation analyses were performed in RStudio (version 2024.04.2+764). Prior to testing, the distributional properties of each variant were tested using the Shapiro–Wilk test for normality. This was done to select the appropriate correlation coefficient. Pearson's correlation coefficient was applied to variables that met assumptions of normality and linearity, whereas Spearman's rank-order correlation was used for variables that were non-normally distributed or ordinal in nature.

For clinical and demographic variables, correlation analyses were performed to examine the relationships among key demographic characteristics and clinical measures, including age, BMI, and relevant cognitive performance and symptom severity scores. These analyses were intended to characterise differences among variables to explore their interrelationships.

- Clinical and demographic variables: Correlations were calculated between demographic/clinical measures (e.g., age, BMI, cognitive and symptom scores) to explore their interrelationships.

- Imaging data: FA values were extracted from clusters showing significant group differences in the TBSS analysis. These values were then correlated with age, BMI, and clinical/cognitive scores to examine brain–behaviour associations.

3 Results

Clinical and behavioural characteristics of the patients are summarised in Table 1. The groups were matched for age and sex, with mean ages ranging from 42.6 to 49.4 years. BED participants had statistically significantly higher BMI (mean = 30.9, SD = 6.6) ($p = 0.003$ (< 0.05)) compared to the GD (25.4 ± 3.6) and control groups (24.8 ± 2.1). The BED participants reported mean duration of problematic binge eating years of 18.1 (SD = 14.9), with an average of 2.2 binge eating episodes per week (SD = 1.8). BED group also had statistically significantly higher Binge Eating Scale (BES) scores with an average of 30.9 (SD = 4.6) ($p = <0.001$ (< 0.05)). The GD and the control groups had scores of 14.4 (SD = 7.8) and 2.8 (SD = 3.1), respectively.

Table 1 Behavioural and clinical information collected from the participants (mean values, (SD)). Abbreviations: AUDIT, Alcohol Use Disorders Identification Test; SOGS, South Oaks Gambling Screen; SD, standard deviation; BIS11, Barratt Impulsiveness Scale; BDI, Beck's Depression Inventory; BES, the Balanced Empathy Scale; DEBQ, The Dutch Eating Behaviour Questionnaire; YALE, Yale Food Addiction Scale; PG DSM-IV, DSM-IV diagnostic criteria for pathological gambling, GD, Gambling disorder; BED, Binge eating disorder; n.a.not applicable
[a]One-way Anova or chi-square test.

	BED	GD	Control	p-value[a]
Number of participants	7	15	17	
Sex (m/f)	0/7	8/7	8/9	0.048
Mean age (SD)	49.4 (5.1)	42.6 (11.8)	43.3 (11.1)	0.35
BMI	30.9 (6.6)	25.4 (3.6)	24.8 (2.1)	0.003
Smoking (y/n)	2/5	11/4	7/10	0.08
Gambling hours per week	0.5 (1.2)	8.7 (7.2)	0.5 (1.2)	0.0003
Gambling euros per week	2.9 (4.6)	152 (149)	3.9 (7.4)	0.001
Problematic gambling years	n.a.	11.6 (7.3.)	n.a.	-
PG DSM-IV points	0 (0)	7.3 (1.4)	0.1 (0.3)	<0.0001
SOGS	0.4 (0.5)	13.3 (2.3)	0.1 (0.3)	<0.0001
AUDIT	3.3 (1.1)	5.9 (4.0)	5.4 (3.3)	0.2
BIS11 total score	65.7 (9.4)	74.2 (5.0)	63.1 (6.4)	0.416
BDI	15.4 (9.6)	14.4 (7.8)	2.8 (3.1)	<0.0001
BES	30.9 (4.6)	4.4 (4.4)	2.1 (2.1)	<0.0001
DEBQ Emotion	50.0 (8.3)	21.2 (8.7)	20.5 (5.0)	<0.0001
YALE	42.3 (6.5)	9.1 (9.5)	5.4 (3.4)	<0.0001
Binge eating episodes per week	2.2 (1.8)	n.a.	n.a.	-
Problematic binge eating years	18.1 (14.9)	n.a.	n.a.	-

3.1 Summary of significant findings

3.2 FA BED > control

The analysis of this data revealed that there were two clusters in the brain with significant differences ($p < 0.05$) between the BED group and the control group, where BED group had higher FA values. These clusters compromised of areas in the internal capsule (Cluster 1) and posterior corona radiata (Cluster 2) (Figure 3; Table 2). No significant findings between any groups in the mean MD, AD, or RD measurement were found.

Cluster 1, where BED group had significantly higher FA compared to control group, consists of 17 voxels in the retrolenticular part of internal capsule, right side (p-value = 0.046 (< 0.05)). Mean coordinates of this cluster were: 59, 93, 8. Thee Cluster 2, where BED group had significantly higher FA compared to control group, consists of 18 voxels in the posterior corona radiata, right side (p-value = 0.048 (< 0.05)). Mean coordinates for Cluster 2 were: 64, 100, 93 (Figure 4). A positive correlation between BES scores and mean FA in this Cluster 2 was also found (p = 0.043).

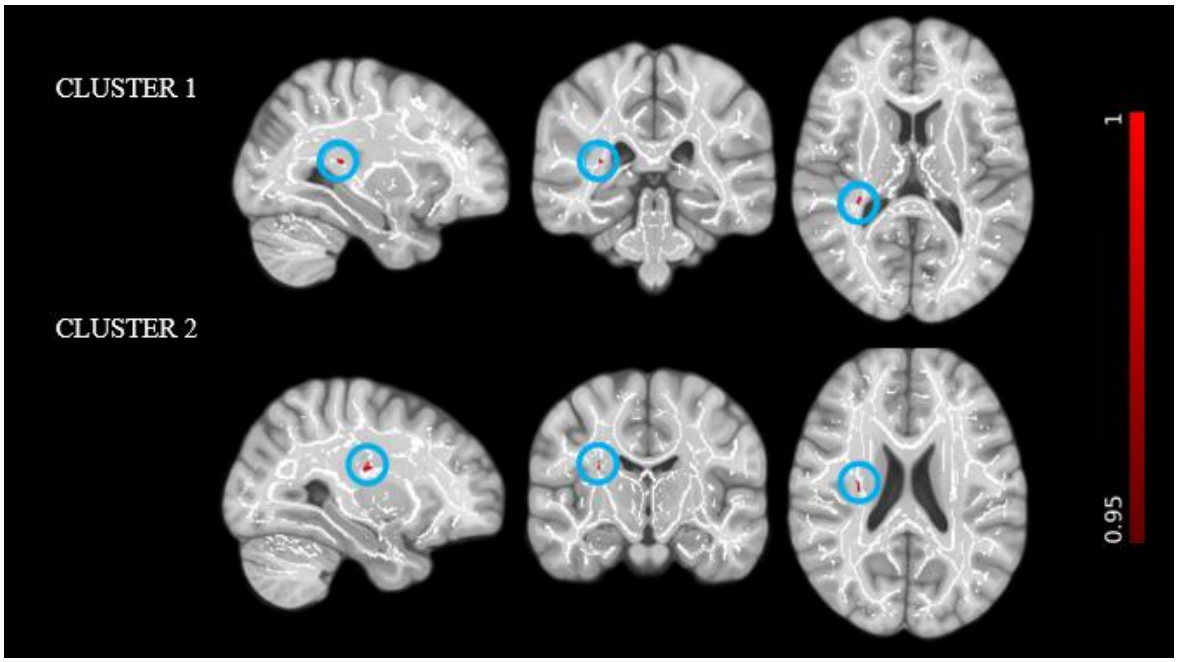

Figure 3: Summary of clusters where the BED participants have significantly higher FA compared to the control group.

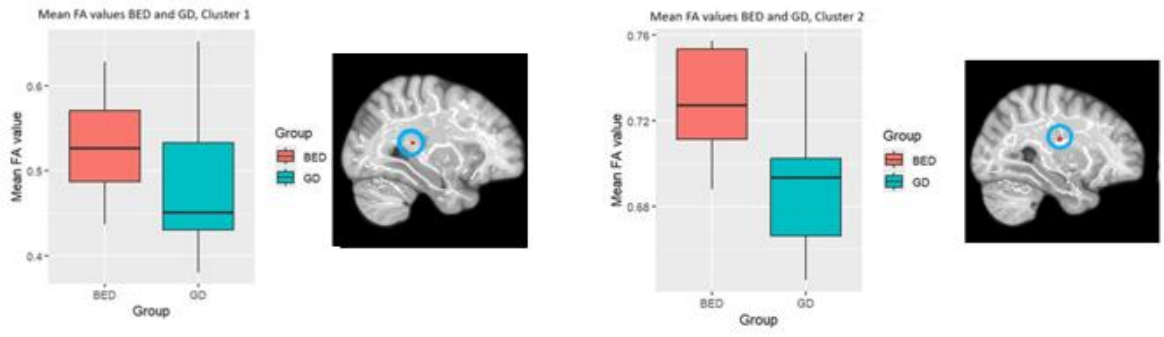

Figure 4: Comparison of mean FA values in cluster 1 and 2 between the BED group and the control group.

Table 2 Summary of significant findings. Abbreviations: BED, Binge Eating Disorder; GD, Gambling Disorder.

		P-value	Region	Number of Voxels
Fractional Anisotropy: BED > control				
	Cluster 1	0.046	Retrolenticular part of Internal Capsule, right	17
	Cluster 2	0.048	Posterior Corona Radiata, right	18

3.3 FA BED > GD

This data showed four different clusters, where the BED participants had significantly higher FA values compared to the GD group. The brain areas covered by these clusters include the body of corpus callosum, retrolenticular part of internal capsule, anterior and superior corona radiata, the posterior thalamic radiation, and the posterior corona radiata, all on the right side. No significant findings between any groups in the mean MD, AD, or RD measurement were measured.

Firstly, Cluster 1, where data shows significant differences in FA values between BED group and GD group, covered the area of anterior corona radiata, right side, and the superior corona radiata, right side. Number of voxels in this cluster were 17 voxels. Maximum p-value was 0.049. The mean coordinates were 70, 144, 100. Cluster 2 with significant differences in FA values between BED group and GD group consisted of the superior corona radiata, right side. Number of voxels in this cluster were 26 voxels. Maximum p-value was 0.048. The mean

coordinates were 61, 111, 93. Cluster 3 covered the area of the superior corona radiata, right side; anterior corona radiata, right side, and the body of corpus callosum, right side. Number of voxels in this cluster were 43 voxels. Maximum p-value was 0.036. The mean coordinates were 72, 138, 103. Cluster 4 consisted of the area of the posterior thalamic radiation, right side; posterior corona radiata, right side, and the retrolenticular part of internal capsule, right side. Number of voxels in this cluster were 289 voxels. Maximum p-value was 0.030. The mean coordinates were 59, 48, 89. A negative correlation between BMI and mean FA values in this cluster ($p = 0.0293$) was also found (Figure 5, 6; Table 3).

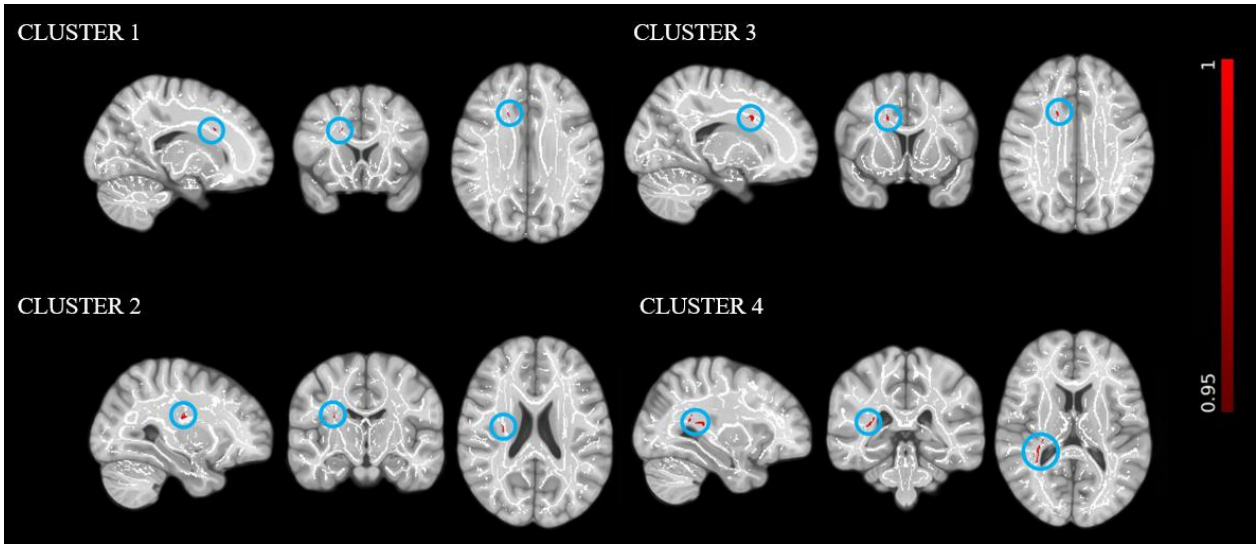

Figure 5: Summary of clusters where the BED participants have significantly higher FA values compared to the GD group.

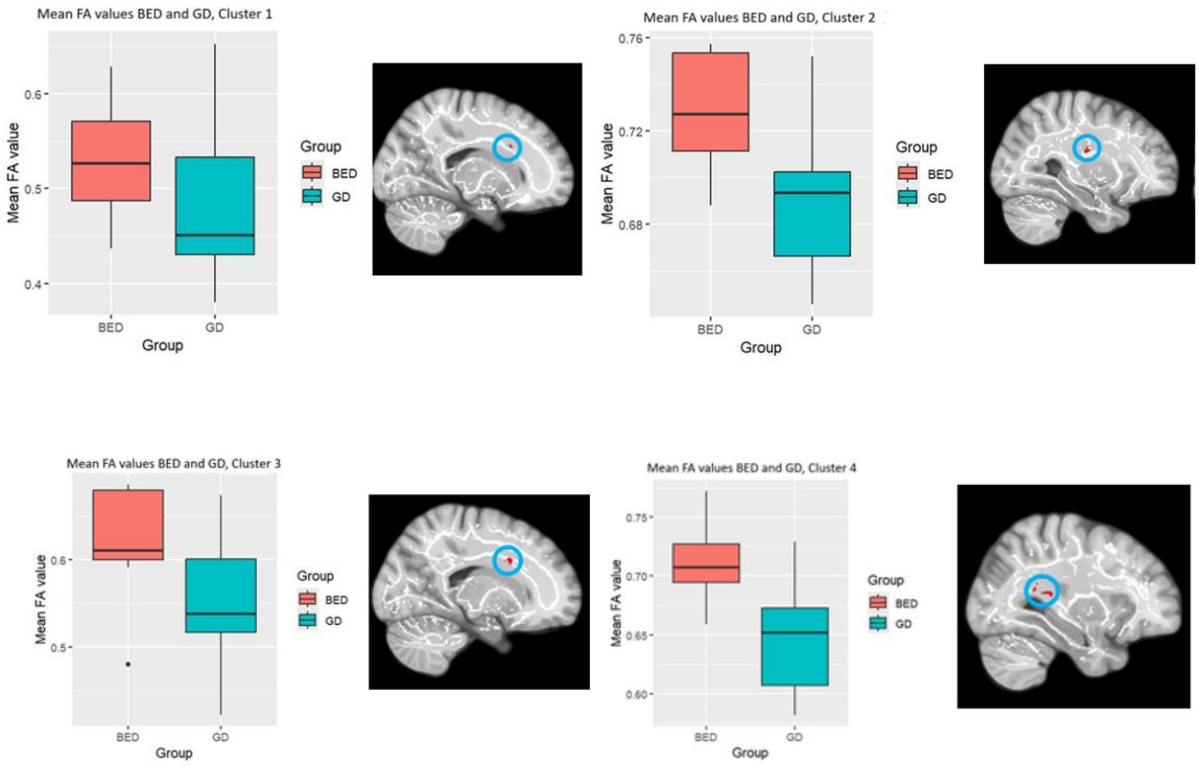

Figure 6: Comparison of mean FA values in Clusters 1, 2, 3, and 4 between the BED group and the GD group.

Table 3 Summary of significant findings. Abbreviations: BED, Binge Eating Disorder; GD, Gambling Disorder.

Fractional Anisotropy: BED > GD		**P-value**	**Region**	**Number of voxels**
	Cluster 1	0.049	Anterior Corona Radiata, right; the Superior Corona Radiata, right	17
	Cluster 2	0.048	the Superior Corona Radiata, right	26
	Cluster 3	0.036	the Superior Corona Radiata, right; Anterior Corona Radiata, right; the Body of Corpus Callosum, right	43
	Cluster 4	0.030	the Posterior Thalamic Radiation, right; Posterior Corona Radiata, right; the Retrolenticular part of Internal Capsule, right	289

3.4 Correlations

3.4.1 Positive Correlation Between BES score and mean FA

The results show a positive correlation between Binge Eating Scale (BES) score and mean FA in posterior corona radiata, R (p-value = 0.043). The BES attempts to measure the severity of the disorder. This indicates that higher BES scores are linked to higher mean FA values (Figure 7; Table 4).

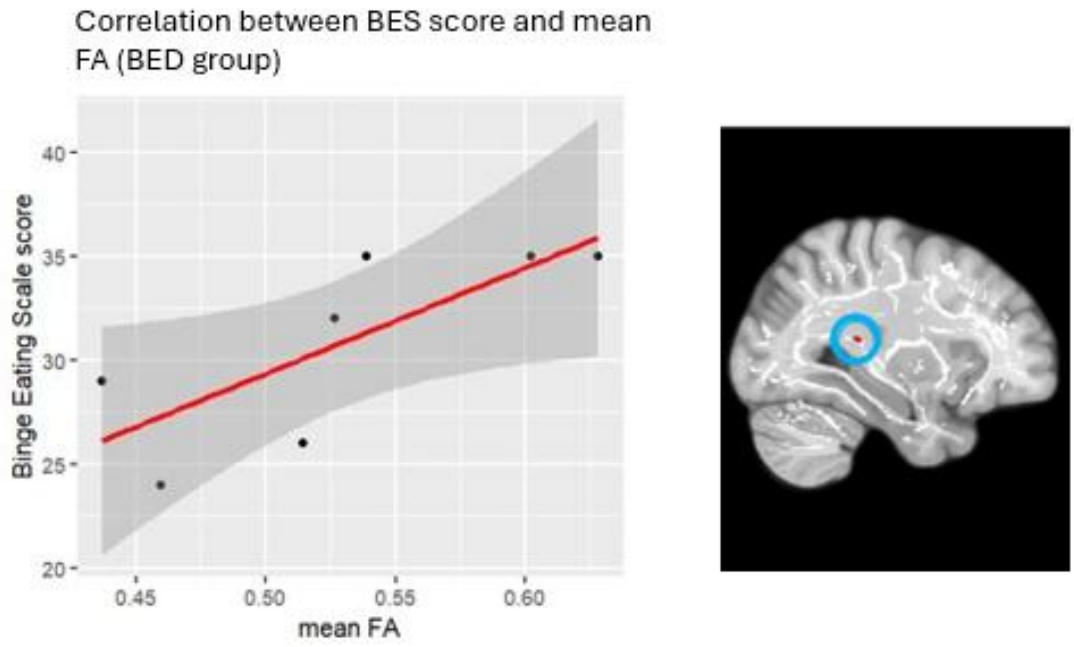

Figure 7: Positive correlation between Binge Eating Scale score (BES) and mean FA in Posterior corona radiata, R.

3.4.2 Negative Correlation between BMI and mean FA

The results indicate a negative correlation between body mass index (BMI) and mean FA in a cluster that involves the retrolenticular part of internal capsule (right side), posterior corona radiata (right side), and the posterior thalamic radiation (right side) (p-value= 0.0219). Therefore, a higher BMI is associated with lower mean FA values (Figure 8; Table 4).

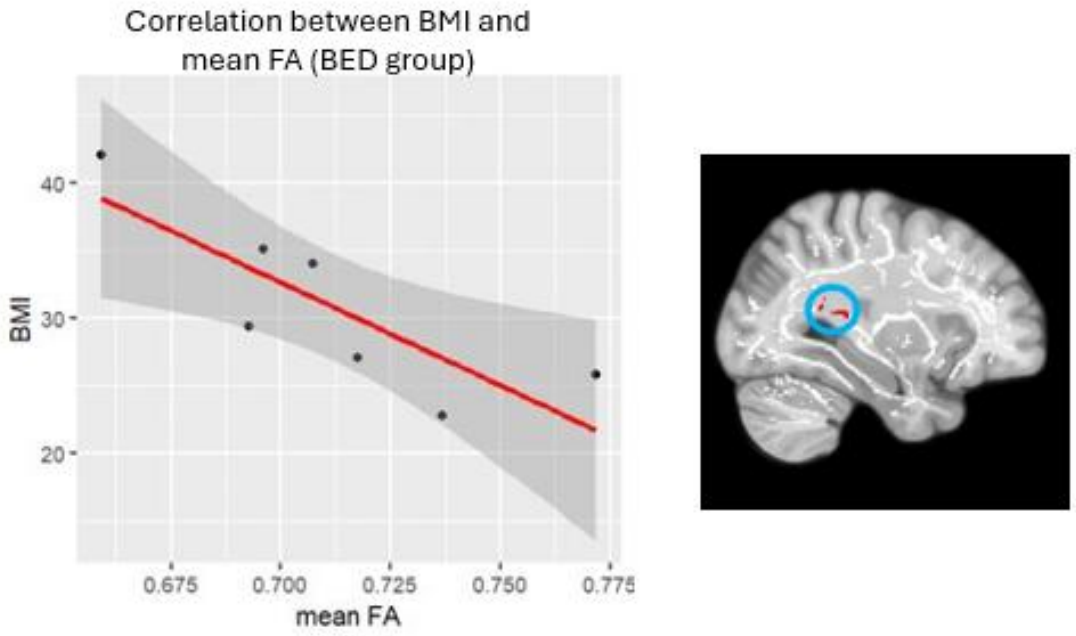

Figure 8: Negative correlation between BMI and mean FA in a cluster comprising of Retrolenticular part of internal capsule, R, Superior corona radiata, R, Posterior corona radiata, R, and Posterior thalamic radiation, R.

Table 4 Significant correlational findings. Abbreviations: BES: Binge Eating Scale; BMI: Body Mass Index; FA: Fractional Anisotropy.

	P-value	**Region**	**Number of voxels**
Correlation between BES and mean FA			
	0.043	Posterior Corona Radiata, right	18
Correlation between BMI and mean FA			
	0.0219	The Retrolenticular part of Internal Capsule, right, Posterior Corona Radiata, right, and the Posterior Thalamic Radiation, right	289

4 Discussion and Conclusions

4.1 Overview of Main Findings

This study examined white matter microstructure alterations in individuals with BED in comparison to healthy controls and patients with GD using DTI. The study examined 39 sex and age matched participants, including 7 participants with BED, 17 control participants, 15 patients with GD. It was expected that BED would express similar white matter alterations that may resemble other behavioural addictions, specifically GD. Furthermore, the BED group was expected to show lowered FA levels compared to healthy controls, as decrease in FA values is commonly observed in other eating disorders, such as BN and Anorexia Nervosa (Donnelly et al., 2018; Gaudio et al., 2019; He et al., 2016). However, contrary to the hypothesis in this study, BED participants were found to showcase increased FA in many brain areas right-laterally compared to both healthy controls and GD participants when controlling for age, sex, and BMI.

The results showed two clusters where BED participants had significantly higher FA compared to healthy controls. Areas in these clusters included the retrolenticular part of internal capsule and the posterior corona radiata on the right side of the brain. The results also showed four clusters where BED participants had higher FA compared to the GD group. The brain areas in these clusters included the anterior corona radiata, the superior corona radiata, the posterior corona radiata, the body of corpus callosum, the posterior thalamic radiation and the retrolenticular part of internal capsule, all of the areas on the right side of the brain.

No significant differences in other DTI measures MD, AD, or RD were observed. Furthermore, elevated FA values correlated positively with BES scores in the posterior corona radiata, and negatively with BMI in a cluster that comprised the retrolenticular part of the internal capsule, superior corona radiata, posterior corona radiata, and posterior thalamic radiation.

4.2 Comparison of BED FA values with other psychiatric disorders

4.2.1 Eating Disorders

Elevated FA was found in multiple tracts among BED participants, including areas of the corpus callosum, internal capsule, corona radiata, and thalamic radiation. This diverges from literature about restrictive eating disorders (Anorexia Nervosa, Orthorexia, Bulimia), which

typically report reduced FA in the corpus callosum, corona radiata, superior longitudinal fasciculus, thalamic radiation, and fornix suggesting compromised white matter integrity (Meneguzzo et al., 2019; Olivo et al., 2017). Although BED is an eating disorder, it seems to exhibit major clinical and neurobehavioural differences compared to other eating disorders, which include restrictive eating disorders such as AN and avoidant/restrictive food intake disorder, and BN, as the core symptoms of BED do not involve purging or restriction of food, at least not the extend as in other eating disorders. Thus, in BED there is an increase in feeding behaviour, whereas restrictive eating disorders are about preventing food intake and BN is characterised by cycle between loss of control around food intake and compensation behaviour to eliminate the intaken food (Frank, 2016; Hay et al., 2017; Reichenberger et al., 2021; Rossi et al., 2023). The divergence from other eating disorder patterns may reflect distinct neurobiological pathways in BED. In particular, BED might involve alterations linked to impulsivity and reward processing, rather than the effects of chronic energy restriction.

4.2.2 Gambling Disorder and Substance Use Disorders

When comparing DTI values between BED and GD groups, it was revealed that the BED participants exhibited increased FA in multiple brain tracts compared to the GD group. These tract areas include the corona radiata, the body of corpus callosum, the thalamic radiation, and the internal capsule.

Addictions, including GD as well as substance use disorders, typically showcase reduced FA in many brain areas, including the corpus callosum, superior longitudinal fasciculus, and the anterior corona radiata (Chamberlain & Grant, 2019). Furthermore, lower FA in GD in the anterior corona radiata and corpus callosum correlates with greater gambling severity (Bellmunt-Gil et al., 2024). Studies also indicate that when substance use disorders and GD are compared directly, they have very similar patterns in terms of white matter alterations, including reduction in FA, possibly suggesting a common neural vulnerability (Yip et al., 2017).

Although BED shares some clinical similarities with addictions, including loss of control over own behaviour and continuation of a behaviour despite harmful consequences, it is possible that it greatly differs from addictions neurobiologically. These disorders may share different adaptations. One possible hypothesis could be that hyperconnectivity has a distinct role in compulsive eating, rather than reward deficiency. There could also be a difference in

reward/control imbalance between GD and BED. In GD, there is impaired connectivity in control networks, whereas in BED there could possibly be an overactive reward drive system.

GD and BED both involve impulsivity-compulsivity continuum. It is possible that although these disorders share similarities clinically, they showcase difference in direction white matter alterations. If BED consistently does not show reduced FA measures, it is possible it cannot be defined as a behavioural addiction despite the clinical similarities.

4.3 Possible interpretations of elevated FA in BED

The findings of increased FA in BED compared to control and GD group are interesting, as psychiatric conditions are usually associated with lowered FA values. White matter microstructure studies on BED are currently very limited.

Estella et al., (2019) found higher FA in the BED participants compared to the obese group in the forceps minor, after controlling for BMI. They also reported increased AD in the forceps minor, anterior thalamic radiation, and superior/inferior longitudinal fasciculi in BED compared to both normal-weight and obese controls, which could indicate broader changes in fronto-limbic and temporoparietal pathways, which could suggest alterations or compensatory mechanisms in decision-making and self-regulation in BED. However, it is unclear if these changes would be the cause or consequence of the disorder, or if they have any clinical significance. This study by Estella et al, (2019) is currently the only published direct and comparable white matter study on BED. Because the research in this area is still very limited, the interpretation of the current results should be considered purely exploratory and tentative, as more research is needed in this area before drawing any certain conclusions.

Although many psychiatric disorders often exhibit lowered FA and decrease in FA indicates disrupted communication between brain areas, it is important to note that increased FA is not always a positive phenomenon, and it can lead to hyperconnectivity. Increased FA can also be seen in cases where there is a compensatory mechanism or over-activation. Compensatory mechanisms can happen similarly to habit formation. This could be a possible hypothesis why BED might exhibit increased FA values in multiple brain areas. Repeated binge eating may increase myelination and over-activation of areas related to, for example, eating behaviour, reward processing or self-regulation. All in all, compensatory strengthening of certain pathways, over-reliance on specific circuits, and reduced adaptability of specific neural networks can lead to cognitive rigidity and impaired flexibility, making it difficult for patients

to change their behaviour. Furthermore, increased reward sensitivity and impulsivity could lead to heightened connectivity in reward and control circuits. In addition, elevated FA is reported in some cases of psychiatric disorders. These include early stages of some disorder, some specific circuits in OCD, addiction, and impulse-control disorders, as well as conditions that involve rigid or habitual processing. Thus, elevated FA in psychiatric disorders is not completely uncommon.

Many studies on eating disorders have also reported differences in FA and other DTI values depending on the stage of the illness. In terms of BED, it could be possible, that degradation, and lowered FA manifests in later stages of the disease. In this study, there was a great variance between participants in terms of problematic binge eating years, the average amount of years being 18.1 years with standard deviation of 14.9 years. In future studies, it could be beneficial to use the stage of illness measured in years of symptoms being present as a covariant to see if the stage of the illness affects the results.

Many areas where this study found increased FA are regions linked to prefrontal and subcortical regions implicated in reward processing, inhibitory control, and emotion regulation (internal capsule, corona radiata, corpus callosum). It could be possible that increased synchronisation between these regions leads to heightened motivation toward food cues. Furthermore, the internal capsule and the corona radiata are both involved in sensory functions. However, more studies are needed to confirm or disprove these speculations.

It is also important to notice that this data did not indicate any differences in other DTI measures, including AD, MD, or RD. Only witnessing changes in FA measures often indicates that the changes are subtle in the fibre architecture. Furthermore, when changes in only FA are present, it suggests that the changes are not damage, but rather adaptation. In terms of BED, this could mean that repeated binge eating behaviour leads to white matter tracts becoming more efficient or specialised.

4.4 Correlational Findings

In this study, two statistically significant correlations were found. Firstly, the data suggests that there is a negative correlation between FA values and BMI, where a higher BMI correlated with a lower FA value in a cluster that covered the retrolenticular part of internal capsule, superior corona radiata, posterior corona radiata, and the posterior thalamic radiation on the right side. This could suggest that higher BMI may be associated with myelination

disruption and thus reduces FA values. Previous obesity studies have consistently shown that individuals who are obese often also exhibit decrease in FA in multiple brain areas compared to individuals who are in a healthy weight range (Daoust et al., 2021; Okudzhava et al., 2022). This could be due to metabolic and inflammatory influences, as higher BMI is associated with chronic low-grade inflammation, metabolic dysfunction, altered lipid metabolism, and insulin resistance, which could all affect myelination and axonal health. However, in this study group, most participants were overweight or obese (BMI > 24.9 kg/m^2), with only two participants being in the healthy weight range. Thus, the BMI range was narrow in BED participants, and BMI was used as a covariate in this current analysis. This is why the observed association should be interpreted with caution, as the restricted BMI range and statistical control may influence the strength of the relationship. Further research may be able to identify whether these kinds of correlations are BED-specific or FA-specific.

Secondly, a positive correlation between FA and BES in a cluster that covered the posterior corona radiata, meaning higher BES scores was found, and thus severity of the illness, correlated with higher FA scores ($p = 0.043$). This could be interpreted as BED severity exaggerating specific white-matter pathways rather than degrade them. Posterior corona radiata is involved in top-down attention, visuospatial processing, and connecting parietal cortex with other regions. Thus, increased FA in this region could mean heightened sensitivity to food cues, exaggerated attentional reactivity, and stronger sensory-reward integration in more severe BED cases. Many studies have shown that individuals with BED have attentional bias towards food cues, which could support the findings of increased FA in this region (Kessler et al., 2016; Werle et al., 2024).

These two correlations seem to create an interesting juxtaposition as patients with BED often have a higher BMI compared to healthy controls. It could be possible that the metabolic and inflammatory effects influence FA in some brain areas, but increased FA in other areas could be something specific to BED and suggest enhanced reactivity toward food cues. This all could support the idea that BED is not simply “an obesity disorder”. Symptoms, such as binging, reward dysregulation, and compulsivity, might have its own influence on the white-matter microstructure of the brain.

4.5 Methodological Considerations and Limitations

The studies on the white matter microstructure in BED are lacking. This current study attempts to breach that existing gap by offering preliminary findings in the white matter

structure in BED. The results attempt to offer an interesting insight into an area that has currently been researched very little.

Currently, only one another study on the white-matter microstructure in BED exists by Estella et al., 2020. Their study on white matter integrity in BED compared individuals with BED to obese individuals and healthy controls. Although they also found increased FA in patients with BED compared to control and obese groups, they also had a relatively small sample group, consisting only of 39 participants with BED, 17 normal weight controls, and 14 obese individuals. Furthermore, as this current study designs differ in terms of comparison groups, it limits direct comparability. Thus, studies with larger patient groups and structured designs are needed in order to understand the white matter changes in BED.

A key limitation in this study is the small sample size. With only 7 BED participants, this study sample is not likely to represent the majority of BED patients. In smaller samples, individual differences can exert a disproportionate influence on group-level results, which may lead to unstable or less reliable estimates of underlying effects. As a result, the observed differences may be driven by variability between participants rather than reflecting robust neurobiological characteristics of BED. Studies with larger sample sizes allow for more reliable estimation of group-level effects by reducing the impact of individual variability. This improves the detection of consistent neurobiological patterns. That is why it is important for future studies to use larger and more heterogenous samples to confirm the robustness and generalisability of the present findings.

Eating disorders often shift over time. For example, it’s very common for people with Anorexia Nervosa later develop BN. It is possible that also people with BED experience episodes of restrictive eating or weight cycling, which might affect white matter in different ways. Thus, changes in white matter might reflect prior diagnosis, not only current BED. Knowing the full medical and psychiatric history of the patient is important for this reason.

In future studies, it is important to determine whether increased FA is something specific to BED. Studies need bigger sample sizes and longitudinal studies are needed in order to understand the effect of the course of the disorder. If increased FA is marked to be something specific to BED, it has potential to be considered as a biomarker for BED. Because behavioural addictions, especially GD, are usually known to exhibit lower FA, this is a possible differentiation of BED from behavioural addictions. It is possible that binge eating

might have cumulative metabolic or neuroinflammatory effects. Longitudinal studies could shed light on to this.

The brain regions where this data indicated significant differences between groups were mainly right lateralised. There is a possibility that this right-lateralisation is due to a statistical phenomenon, but it is interesting that in the study by Estelle et al., (2019) findings were also right lateralised. Again, it is possible that that is just an anatomical variation amplified by TBSS skeletonization and a phenomenon due to statistics. Despite all of this, finding being right-lateralised is a common finding for reward and impulse-control networks, and this pattern needs replication with future studies.

Furthermore, BED diagnostics are heterogenic, meaning BED varies in severity, chronicity, emotional eating profiles, impulsivity, and comorbidities. It is possible that FA values differ and might reflect the state, trait, or mixed neurobiological factors. Furthermore, studies on the subject differ a lot so it is difficult to compare them. Many studies only study obese participants with BED, which might not give a full representation of people with BED, as many patients are normal weight, at least at the beginning of the disorder.

TBSS is often used in DTI research. Although it is commonly used, it has its downfalls. For example, TBSS skeletonization loses peripheral white-matter information. TBSS is sensitive but it is also only voxel wise specific which might limit it to major tracts. Furthermore, registration inaccuracies might blur tract boundaries, meaning non-related brain areas might be involved in clusters that are labelled as significant. Also, crossing fibres might cause misleading FA increases of decreases. Thus, although results are interesting and shed a new light into an area that has not been greatly researched before, the results need to be replicated in later studies.

Lastly, addiction and psychiatric disorder research is in itself challenging. Impulsivity, reward sensitivity, and compulsive behaviour all overlap but are measure differently across disorders. Furthermore, comorbidities can cloud interpretation of results. However, this study already was controlled for other psychiatric disorders. It is important to continue that protocol in future studies. Also, individuals with addiction disorders might be unreliable in attending research studies that require multiple times of attendance.

4.6 Implications and Future Directions

As mentioned previously, the results from this study are purely preliminary and only based on a small group of people. However, if future studies indicate similar findings, these results support the theory that there is a structural involvement of reward and control circuits in BED. However, before these kinds of claims can be made, multimodal and longitudinal studies are needed with diverse and large sample sizes. Especially more research on the male population with BED should be conducted in order to get more empirical evidence in terms of brain alterations. Currently, most investigations on BED have studied the female population.

Clinically and treatment wise, studying white matter and finding significant differences between disorder might have implications for treatment. If changes in white matter structure, for example, suggest that there is hyperactivity of brain areas involved in food cues, it could have a significant role in treatment. Furthermore, in eating disorder research, generally it seems that long-term recovery normalises alterations in FA, meaning patients with previous eating disorder, do not have significant differences in brain white matter compared to healthy controls. There is currently no data on whether white matter alterations in BED change after recovery, but in the future, it could be beneficial to research how recovery and possibly normal weight maintenance affects white matter integrity in individuals with BED.

Since BMI and BES in this data show opposite associations with FA, future work could investigate BED-specific neural mechanisms independent of weight. Ideally, future studies would include weight matched non-BED controls which could help clarify if the results of possible elevated FA are driven by binge eating, compulsivity, reward sensitivity, or metabolic variables. Furthermore, including behavioural and task-based measures related to reward, impulsivity, or cure reactivity could offer valuable insight into why BED might have elevated FA in specific brain regions.

BMI seems to play a great role in BED research. BED often leads to higher BMI but currently it seems that white matter changes in BED are different from those who are overweight or obese without having BED. Thus, having studies where participants are BMI-matched and metabolic controlled could help with separating BED effects from the effects of having a high BMI.

Many DTI studies lack standardised pipelines. In this current study, QSIprep was used to preprocess the data. QSIprep automates and standardises the preprocessing pipeline, which is

a step forward in comparability across studies. However, currently, there is a lot of variances in preprocessing, acquisition parameters, and pre-registered hypotheses. To ensure comparability in the future, these steps should be standardised.

It is important that future studies use multi-modal, hypothesis-driven region of interest analysis. For example, white matter bundles with fronto-limbic connections could be targeted. Furthermore, structural differences should be linked to fMRI resting state networks, reward-related activation patterns, and cognitive performance, such as inhibitory control tasks to ensure multimodal approach.

4.7 Conclusion

This thesis examined white matter microstructure in BED to clarify its neurobiological profile by comparing diffusion imaging measures across individuals with BED, GD, and healthy controls. By situating BED alongside GD, which is a behavioural addiction, and a non-clinical control group, this study aimed to better characterise whether BED exhibits distinct or overlapping patterns of white matter organisation. The present findings contrast with findings from studies on other psychiatric disorders, including behavioural addictions. This could indicate that BED has unique neurobiological framework. Given that white matter microstructure in BED has received relatively limited empirical attention, this study offers novel insight into this area.

Individuals with BED demonstrated consistently higher FA compared to both healthy controls and the GD group. The effects were localised to right-hemispheric white matter pathways. The areas where BED showed increased FA (corona radiata, internal capsule, posterior thalamic radiation, and corpus callosum) consisted of white matter pathways supporting cortical-subcortical connectivity. No significant group differences emerged in other diffusion measures, suggesting the changes are subtle and organisational rather than damage to the tissue. Additionally, FA values were positively correlated with BES scores in the posterior corona radiata and negatively correlated with BMI in a cluster spanning the retrolenticular internal capsule, superior and posterior corona radiata, and posterior thalamic radiation. Future studies could focus on not only on examining the white matter changes in BED, but also to determine if these results represent a characteristic unique to BED, potentially through compensatory adaptation, altered developmental trajectory, or experience-dependent plasticity.

Future research may build on these results by examining white matter alterations in larger and more heterogeneous sample groups. Furthermore, these findings could aid in exploring possible biomarkers for BED. By demonstrating distinct patterns of white matter organisation in BED, this study contributes to an area of research that has not been excessively studied and contributes to a more nuanced understanding of BED's neurobiological underpinnings. It is important to continue investigation of network-level brain differences in BED to refine theoretical models of BED and to inform more targeted and disorder-specific research approaches.

Acknowledgments

Thank you for your guidance, expertise, and your never-ending patience Juho Joutsa and Albert Bellmunt-Gil, as well as the whole Turku BRAINLAB staff and researchers. The data for this study comes from a study by Majuri et al., 2017, so I would like to thank them for even making this project possible. I would also like to thank the University of Turku and the Human Neuroscience program for allowing me to study this fascinating subject. I'm also grateful for my family, friends, and the health professionals that supported me through this journey and during difficult periods. Special thank you to my therapist, who always told me that despite everything, I could finish my thesis and graduate. Tessa and Steven, my cats, also deserve an honourable mention. At this point they should both have a neuroscience degree as well.

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