Gambling, alcohol and gender: Subjective effects and clinical characteristics

Louise Miller

Department of Psychiatry and Neurochemistry
Addiction Biology Unit
Institute of Neuroscience and Physiology
Sahlgrenska Academy, University of Gothenburg, Sweden

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louise.miller@neuro.gu.se
louisemiller27@hotmail.com

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To my parents for your never ending support.

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ABSTRACT

Gambling and alcohol are two recreational activities enjoyed by many people all over the world. Most with the purpose of leisure and social interaction with little or no consequence to impact daily life. For some however these activities can lead to harmful use and addictive tendencies can develop. This thesis explored the subjective effects of gambling within a recreational groups of gamblers, non-gamblers and those who experience a 'high' from the activity, also referred to as 'high gamblers'. The aim was to establish how a healthy population responded when exposed to a gambling challenge. The groups were further split into gender to examine whether any differences were seen between men and women as previous literature has demonstrated a male dominancy. Since there are limited population studies exploring the treatment seeking population for gambling addiction we investigated which demographic groups are seeking treatment. Further we explored the subjective effects of alcohol across different age spans to gain a broader perspective of the effects of alcohol and whether alcohol use disorder was a risk at different ages.

We found that high recreational gamblers reported more stimulative effects of a gambling challenge compared to those who gamble little or not at all (**Paper I).** Further when exploring gender differences, we found that both men and women reported stimulatory effects from the gambling challenge, but no differences in the subjective effects were found between genders. However the men showed an increase in systolic blood pressure compared to women after the gambling challenge **(Paper II).** We also found clinical differences between men and women with gambling disorder. We found that men and women differed in age, living situation, harmful alcohol use, problematic drug use and comorbidity **(Paper III).**

We also explored the subjective effects of alcohol with regards to age and gender and found that both older and younger subjects showed increased stimulatory effects after a moderate dose of alcohol. When looking at gender we found that women showed decreased feelings of tension and anger compared to men **(Paper IV)**.

In conclusion, this thesis strengthens the addictive tendencies of slot machine gambling as seen by subjective higher arousal effects. Gender differences in a stimulatory response of a gambling challenge were not seen which is a unique outcome in comparison to existing literature. However we found gender differences in a patient population. Alcohol use across different age spans showed that men wanted to drink more and that the different subjective effects were seen between gender and age groups. This highlights the risk for alcohol use disorder independent of age.

Keywords: Addiction, Alcohol, Gambling, Gender, Subjective effects.

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SAMMANFATTNING PÅ SVENSKA

Spel- och alkoholberoende är idag psykiatriska diagnoser. I Sverige har cirka 2% av befolkningen ett spelmissbruk och inom vissa mindre grupper med psykiska problem eller hos interner är andelen mycket högre. I dagsläget tros cirka 0,8% män och 0,2% kvinnor ha ett spelmissbruk i Sverige. Gällande alkoholberoende är det ungefär dubbelt så många 4% som har detta fördelat på cirka 4% män och cirka 3% kvinnor.

Likheterna mellan en person som är beroende av alkohol eller spel är många. Båda typerna av beroende visar på förändringar i belöningssystemet sett i fMRI studier, de uppvisar tolerans och abstinens samt att de försöker sluta utan att lyckas. Alkohol- och spelberoende delar även flera liknande neurobiologiska, psykologiska och fysiologiska förändringar. Just därför representerar individer som spelar mycket en viktig subgrupp inom missbruksforskningen. Stora likheter ses även gällande den subjektiva upplevelsen av spel och alkohol. En liknelse är att spelmissbrukaren som till exempel ser en film med scener från ett casino upplever stimulering på liknande sätt som en alkoholberoende person upplever då hen ser en film med scener från en bar. En annan liknelse är att en spelsituation påverkar signalsubstansen dopamin som är en känd markör i ett missbruk. Idag vet man även att den som spelar visar ökad puls, blodtryck och ökade svettningar när de spelar. Annars är de initiala effekterna av spelande i stort sett okända. Tidigare studier är få och reflekterar lite över samsjuklighet med sjukdomar som till exempel alkohol och drogproblem. Studierna är oftast epidemiologiska och är inte utförda i en kontrollerad laboratoriemiljö.

I denna avhandling anskaffar vi ny kunskap genom kontrollerade experimentella situationer där friska spelare utan spelberoende får spela om pengar i laboratoriemiljö samtidigt som vi studerar subjektiva och fysiologiska förändringar med väletablerade mätmetoder och

mångårig erfarenhet från vårt human experimentella laboratorium. Om det visar sig att spelandet, hos individer utan ett spelberoende, aktiverar vårt belöningssystem och ger en ökad känsla av välbefinnande finns det en möjlighet att belöningssystemet har omstrukturerats och mekanismer involverade i utveckling av beroende initierats. I **Paper 1** fann vi bland annat att ”high recreational gamblers” upplevde spelsituationen som mer stimulativ än personer som inte spelar alls. Det kan vara så ett ihärdigt spelande även ökar risken för att utveckla ett beroende till framför allt alkohol, en av världens stora folksjukdomar. I detta experiment studerade vi även om det föreligger skillnader mellan män och kvinnor i deras subjektiva upplevelse av spel. I **Paper II** fann vi att både män och kvinnor subjektivt upplever stimulation efter spelandet på samma sätt. Vi såg därmed inga skillnader mellan könen. Då vi fann en aktiveringen av belöningssystemet efter spelande även är subjektivt mätbart finns det goda grunder till att kunna utveckla både preventiva metoder och behandling av spelmissbruk.

På samma sätt studerar vi även de subjektiva effekterna av moderat dos av alkohol och hur det påverkar olika åldersgrupper och om det finns några skillnader mellan könen. I detta experiment utgår vi från liknande hypoteser att de subjektiva effekterna av alkohol i förlängningen kan påverka hur en man eller en kvinna i en viss åldersgrupp konsumerar alkohol. I **Paper IV** fann vi att både yngre och äldre personer upplevde subjektiv stimulering av alkohol och att yngre personer samt kvinnor upplevde minskad spänning och oro efter alkohol. Vi anskaffar oss även ny kunskap genom kliniska observationer av individer med spelmissbruk som söker vård på för sitt spelberoende. Genom kliniska observationer av spelmissbrukare studerar vi även könsskillnader. Genom skattningsskalor som mäter samsjuklighet, spelberoende, alkohol- och drogproblem, livskvalitet, samt möjliga vägar in i ett beroende. Idag finns få kliniska studier gjorda mellan vårdsökande spelberoende män och kvinnor i Sverige. Vi fann bland annat i **Paper III** att spelberoende kvinnor

oftare än män var ensamstående föräldrar och led av ångest och depression. Männen däremot led oftare av alkohol- och drogproblem. Vi såg även att männen var cirka 5 år yngre än kvinnorna och att de började spela cirka 10 år tidigare än kvinnorna. Vi kan genom dessa observationer närma oss den här gruppen och på så sätt i framtiden utveckla bättre och mer specifika behandlingsmetoder och strategier för både män och kvinnor.

LIST OF PAPERS

This thesis is based on the following papers referred to in the text by their Roman numerals.

I. **Miller L,** Gordh AS. High Recreational Gamblers Show Increased Stimulatory Effects of an Acute Laboratory Gambling Challenge. J Gambl Stud. 2021 Mar;37(1):299-318. doi: 10.1007/s10899-020-09952-3.

II. **Miller L**, Söderpalm Gordh A. Subjective and Cardiovascular Responses to an Acute Laboratory Gambling Task in Men and Women. Front Psychiatry. 2022 Jun 6;13:702298. doi: 10.3389/fpsyt.2022.702298.

III. **Miller L**, Mide M, Arvidson E, Söderpalm Gordh A. Clinical differences between men and women in a Swedish treatment-seeking population with gambling disorder. Front Psychiatry. 2023 Jan 4;13:1054236. doi: 10.3389/fpsyt.2022.1054236.

IV. **Miller L**, Söderpalm Gordh A. The effects of age and gender on subjective responses to alcohol. *Submitted 2023.*

CONTENT

ABBREVIATIONS

ABU	Addiction Biology Unit
ADHD	Attention-Deficit/Hyperactivity Disorder
AMPH	Amphetamine
APA	American Psychiatric Association
ARCI	Addiction Research Centre Inventory
AUD	Alcohol Use Disorder
AUDIT	Alcohol Use Disorders Identification Test
BMI	Body Mass Index
DEQ	Drug Effect Questionnaire
DSM-5	Diagnostic and Statistical Manual of Mental Disorders
EGM	Electronic Gaming Machine
GD	Gambling Disorder
GLM	Generalized Linear Model
ICD-10	International Classification of Diseases and Health
PGSI	Problem Gambling Severity Index
SEM	Standard Error of Means
SD	Standard Deviation

SPSS	Statistical Package for Social Sciences
SUD	Substance Use Disorder
VAS	Visual Analog Scale
VGR	Västra Götaland Region
WHO	World Health Organisation

INTRODUCTION

My background: Nutrition, food addiction, alcohol addiction and my way into psychiatry, alcohol, gambling and exploring subjective effects.

I spent most of my academic life within health science in nutrition and dietetics before moving into gambling and alcohol research. Previously I had a real interest in people who were addicted to food and suffered with binge eating and eating disorders. There was something about their behavior that I found fascinating and I wanted to know more about human behavior and addiction. Food addiction often stems from highly palatable foods that are usually processed and high in salt, sugar and fat, they are usually not found in nature. The Yale food addiction scale (Gearhardt et al., 2016) has been used in studies that look at food addiction and it has been able to draw a comparison between other addictions, for example drugs and the neurobiological mechanism that it has in common with both behavioral addictions (Lindgren et al., 2018, Laque et al., 2022). This is an interesting link and pathway into the reward system, experiencing excitement and pleasure and the link into other behavioral addictions like gambling (Etxandi et al., 2022).

Research has been able to show that there is an overlap between specific areas of the brain and behavioral addictions such as for example the consumption of highly addictive foods (Bijoch et al., 2023). Similarly the consumption goes through a withdrawal process similar to addictive drugs once the path to abstinent is undertaken. This again is seen in alcohol and drug addiction but interestingly also in food addiction (Parnarouskis et al., 2022).

In a deviation from nutrition, I found a project that really took my interest into a new area of addiction and delved into the world of online gambling addiction and looking at human behavior along with the

differences within the genders and the roll that the subjective effects play.

HISTORY OF GAMBLING

Gambling has been a part of human society for thousands of years. Dating all the way back to 2300BC in ancient China, where tiles were discovered which were thought to have been used for a rudimentary game of chance (Childs, 2008). Throughout history, gambling has been seen as both a form of entertainment and a way to win money. In medieval Europe, games of chance, such as dice and cards, were popular among the nobility. Another milestone in more recent times was the development of casinos in 1638, when the Ridotto was founded in Venice to offer a controlled gambling environment (Childs, 2008). From then on all over the world casinos and gambling became mainstream. In more recent times online casinos and online gambling have become big business. In 1994 the first online gambling company began and since then it has spiraled out of control (Munting, 1996). Gambling however remains controversial in some groups but continues to be a widespread and a popular form of entertainment for many.

The first online gambling club was called "The Gaming Club" and was operated by Microgaming, a software company based in the Isle of Man, United Kingdom. The Gaming Club offered a limited selection of casino games such as blackjack and roulette, but it paved the way for the online gambling industry that we know today (D'Addario, 2012). Initially gambling within an online forum was met with scepticism and harsh regulation challenges especially in countries like the United States. The Department of Justice took a hard-line stance against online gambling and made the regulations difficult (Berzon, 2011). However by the late 1990s gambling on an online forum had

gained immense popularity particularly in Europe where it was more widespread and readily accepted (D'Addario, 2012).

With the introduction of secure online payment systems and ever increasing advancements in technology including the development of smart phones, tablets and available interfaces together with faster internet speeds, this combination made the growth of the online gambling industry explode. Today, online gambling is a multi-billion dollar industry with thousands of online casinos, sports books, and poker rooms operating globally (McBride and Derevensky, 2012). Despite its popularity, online gambling remains a controversial topic, with some critics raising concerns about problems related with gambling, underage gambling, and the potential for fraud and money laundering. As a result, online gambling is heavily regulated in many countries as discussed earlier in the USA, with operators required to obtain licenses and follow stringent guidelines to safeguard fair and responsible gambling.

Gambling Disorder

Some individuals that gamble regularly may start to experience addiction-like symptoms, such as craving and loss of control, when engaging in gambling activities. These individuals may prioritize gambling over other important aspects of their lives, such as work, family, and social relationships, leading to negative consequences and gambling disorder (Moreau et al., 2020).

Gambling disorder is a behavioral addiction that is indicated by a continued, persistent, excessive, impulsive, and uncontrollable participation in an activity or action despite the negative outcomes or impacts (American Psychiatric and American Psychiatric Association, 2013). Gambling disorder was introduced into The Diagnostic and Statistical Manual of Mental Disorders 5th Edition (DSM-5; American Psychiatric Association, 2013) in 2013 by the American Psychiatric

Association (APA) (American Psychiatric and American Psychiatric Association, 2013). The inclusion of gambling disorder in the DSM-5 marked an important advance in the field of psychiatry. Prior to the DSM-5, gambling was considered an impulse control disorder, and not as a substance-related addiction, and was categorized and known as "Pathological Gambling".

However, research and clinical evidence continued to find over the years that gambling disorder shared several comparisons with substance-related addictions (Rash et al., 2016). These included; changes in brain activity, cravings, tolerance, and withdrawal symptoms (Limbrick-Oldfield et al., 2017, Hasanović et al., 2021). These findings led to a re-evaluation of how gambling-related problems should be classified and diagnosed. Gambling disorder includes nine criteria as listed in Table 1. As previously described gambling disorder shares similarities to alcohol use disorder (AUD) and substance use disorder (SUD).

Table 1. DSM-5: *The diagnosis of gambling disorder requires at least four of the nine criteria to be fulfilled. The severity of the disorder can be classified as mild (four to five criteria met), moderate (six to seven criteria met), or severe (eight to nine criteria met). (American Psychiatric and American Psychiatric Association, 2013).*

Table 1.

Diagnostic criteria for gambling disorder according to the DSM-5

1. Needs to gamble with increasing amounts of money in order to achieve the desired excitement.

2. Is restless or irritable when attempting to cut down or stop gambling.

3. Has made repeated unsuccessful efforts to control, cut back, or stop gambling.

4. Is often preoccupied with gambling (e.g., having persistent thoughts of reliving past gambling experiences, handicapping or planning the next venture, thinking of ways to get money with which to gamble).

5. Often gambles when feeling distressed (e.g., helpless, guilty, anxious, depressed).

6. After losing money gambling, often returns another day to get even ("chasing" one's losses).

7. Lies to conceal the extent of involvement with gambling.

8. Has jeopardized or lost a significant relationship, job, or education or career opportunity because of gambling.

9. Relies on others to provide money to relieve desperate financial situations caused by gambling.

**Adapted from the DSM-5*

Gambling prevalence

The prevalence of gambling varies depending on the country and region, as well as the type of gambling being considered. In general, gambling is a popular form of entertainment worldwide, with many people participating in various forms including betting on the lottery, visiting casinos, placing sports bets, and partaking in online gambling including slot machines (Booth et al., 2021). The most popular type of gambling for adult's in general is the lottery (Booth et al., 2021). The lottery is considered to be a less harmful form of gambling and is considered very socially acceptable to be involved in. Sports betting, casino gambling, electronic gaming machines (EGM) and horse betting are also very popular however, these have a much higher level of gambling related harm when looking at problematic gambling behavior (McCarthy et al., 2018, Booth et al., 2021).

Globally gambling has been considered to be a public health problem with the prevalence of problem gambling ranging around 0.5-7.6% (Mora-Salgueiro et al., 2021, Gartner et al., 2022). The World Health Organization (WHO) reported that 80% of global gambling spending (user losses) is on land-based activities for example at casinos, sports betting, horse racing and playing the lottery. However, online participation and spending have increased distinctly, for example in Sweden half the market is now online (Abbott, 2020).

The Asia-Pacific region is the largest gambling market in the world, with countries like China, Japan, and South Korea having a long history of gambling culture (Xue et al., 2021). In Europe the highest gambling participation is seen in the UK with one report finding that 65% of English and Scottish adults who were over the age of 16 participated in some form of gambling within the last year. The split between the genders showed that 68% were men and 62% were women (Seabury and Wardle, 2014). Gambling in the United States is a very popular activity, where around 75% of adults have gambled at least once in their lifetime, with the most popular form of gambling being the

national lottery with one study showing 66% of their national survey reported playing the lottery on a regular basis (Welte et al., 2002).

In Sweden around 2.1% of the population has been predicted to have some sort of gambling addiction and approximately 0.6% experience sever gambling problems (Abbott et al., 2018). The prevalence of problem gambling within Sweden was first reported in SWEGS in 1998 (Volberg et al., 2001). There have been more studies reporting the prevalence in Sweden with SWELOGS (2015, 2018, 2021) (Folkhalsomyndigheten, 2021). In the clinical population a much higher prevalence of gambling problems have been found, ranging between 6%-23% (Nehlin et al., 2016, Cowlishaw et al., 2014).

Etiology of gambling

The complexity of the etiology of gambling is a multi-faceted phenomenon that combines a diverse range of biological, social, environmental and psychological aspects. The exact cause of gambling or gambling disorder is not well understood and many theories have provided explanations as to why some individuals may be more incline to progress into gambling disorder. Previous research has shown that having a family history of gambling disorder may have some influence on the individual's likelihood to develop problematic gambling behavior (Dowling et al., 2021, Petry et al., 2018, Gyollai et al., 2014, Ibáñez et al., 2003). More research is however needed as the existing studies are preliminary and need more in-depth exploration to understand this genetic connection.

It has been seen that environmental and social factors allowing accessibility to gambling can influence the likelihood of developing gambling disorder (Parodi et al., 2017). Cultural attitudes towards gambling are also a contributing factor, as is the degree to which an individual is exposed to frequent gambling advertising and living in areas that have a greater availability of gambling options (Syvertsen et

al., 2022, Donaldson et al., 2016). Further in a meta-analysis that reviewed twin studies found that gambling was influenced by age, gender, genetics and environmental factors (Xuan et al., 2017).

Social surroundings

The surrounding social environment has been known to have a contributing factor when looking at addictive behaviours. It has been seen that family and social peer groups can have a contributing factor that influences how people behave and what they are subjected to in their surroundings. Previous research has demonstrated that these social influences of peers and family, especially parental figures have had a role in the development of certain gambling behavior and activities (Awaworyi Churchill and Farrell, 2020). Social factors such as peer pressure, a culture of gambling, and accessibility to gambling can increase the risk of developing a gambling problem (Raylu and Oei, 2002). On the other hand, previous literature has reported that social isolation and loneliness have also been considered motives for gambling behaviours (McQuade and Gill, 2012, Castrén et al., 2013).

Age

Young people are at a higher risk of developing a gambling problem because they are more likely to engage in risky behaviours and have less developed decision-making skills (Páez-Gallego et al., 2020). Boredom has also been listed as a reason to participate in gambling as well as the motive to "get rich" (Treglia, 2021, Donati et al., 2021). Psychological wellbeing also has an impact on decision making and can attribute to decisions around partaking in gambling or other risky activities (Páez-Gallego et al., 2020).

Gender

Men are more likely to develop gambling problems than women, although the gender gap is narrowing. As reported in **Paper I and II** men have more often been represented as the dominant groups that demonstrates problematic gambling behaviour. Previous research has strongly suggested that men gamble more than women, however it has now been seen that women are "catching up" and they progress to problematic gambling faster than men. However, women seek treatment earlier and begin to gamble due to anxiety and depression, which is opposite for men who become depressed due to their excessive and problematic gambling behaviour **(Paper III)**. Women are typically older than men when they begin to gamble and often live alone or are single parents. Men however are more often married or living with a partner (Ronzitti et al., 2016, Lahti et al., 2013, Echeburúa et al., 2011)**(Paper III)**.

Comorbidity

Psychological and psychiatric factors such as impulsivity, anxiety, depression, and substance abuse, have been associated with an increased risk of developing a gambling problem (Hing and Russell, 2017). It has been seen that the use of alcohol, cannabis and substance use have been common foundations of certain personality types that are attributed to being more at risk of gambling disorder (Dash et al., 2019, Sundqvist and Rosendahl, 2019). Those who have a predisposition to act impulsively or seek out intense experiences may be more inclined to engage in gambling behaviour (Ring et al., 2022). Additionally, individuals who have cognitive distortions, for example believe that they can control the outcome of a game, may be more prone to developing gambling problems. There is also a tendency to chase losses in an attempt to obtain control over their behaviour (Chen et al., 2022, Auer and Griffiths, 2022).

Overall, the etiology of gambling is complex and multifaceted, a combination of these risk factors contribute to the development of gambling disorder in vulnerable individuals (Williams et al., 2023).

Individual Responses

Theories of continued use

The majority of people would not consider the choice to experiment with drugs, however for those who do, the number that continues to use is very few and the ones who become addicted are even smaller. Some move on to recreationally use drugs with little impact to their functioning life, without abuse or a dependency issue developing. It has been shown that how a person responds to an initial exposure to a drug can determine the likelihood of the abuse tendency (de Wit and Phillips, 2012, Haertzen et al., 1983). A lot of drugs that have the potential of abusive tendencies produce subjective feelings of well-being and euphoria in humans, this is believed to contribute to the drug's possible potential for abuse or misuse (de Wit and Griffiths, 1991, Fischman and Foltin, 1991). The mood-altering and subjective effects have been seen to determine whether continued use or abuse will endure outside of the first exposure however an individual's response to a drug can vastly differ between people (Fischman and Foltin, 1991, de Wit and Phillips, 2012).

Subjective responses to alcohol

Studies investigating alcohol have established that individuals exhibit variations in their subjective responses when engaging in drinking behavior. One theory suggested that a low level of reaction**,** for example subjective behavioral reactions to alcohol, impacts an

individual to drink more and predicts a risk for progressing into alcohol use disorder (Schuckit, 1994). A later theory suggests that the experience of positive and stimulant-like effects of alcohol, to a higher levels of drug enjoyment and euphoria, subsequently motivated the individual to consume greater quantities of alcohol (de Wit et al., 1987, Chutuape and de Wit, 1994). Furthermore in a five year follow up study, a higher rather than a lower reaction to alcohol indicated the onset or likelihood of alcohol use disorder developing. This effect was explicitly seen in heavy drinkers (King et al., 2014).

Physiological responses to gambling

It is not clearly understood why some people intensify their gambling behavior whereas others do not. However, there are theories that physiological arousal holds a significant role to both the instigation and continuation of gambling behaviors. Previous research has demonstrated that gambling can trigger an increase in physiological responses.

In the early 1980, it was found that in a group of students and in a group of regular gamblers both showed increased heart rate while playing black jack in a real life case scenario and in a laboratory casino. They also found that the increase in heart rate was more prominent in the real life casino setting compared to the laboratory (Anderson and Brown, 1984). Later, heart rate was measured in regular gamblers and in gambling addicts playing on a slot machine in the laboratory. It was found that gambling initiated an increase in blood pressure although no difference was seen between the groups (Carroll and Huxley, 1994). Further, in a pilot laboratory study heart rate and blood pressure was measured in compulsive gamblers compared with controls while listening to tapes of their preferred form of gambling. The compulsive gamblers showed a significant increase in heart rate as a response to

the gambling audio listening in comparison to the controls (Blanchard et al., 2000).

Subjective responses to gambling

Similarly to alcohol, it has been documented that gambling also elicits subjective effects in both real life case scenarios or in the laboratory.

The role of subjective mood has been investigated in the use of a fruit machine gambling behaviour. Griffiths (1995) showed that in pathological gamblers and regular gamblers, gambling on a fruit machine triggered a person to feel 'high' and aroused compared to non-gamblers. It was also found that regular and pathological gamblers experienced more depressive moods initially before playing on the fruit machine (Griffiths, 1995).

Further, a study compared pathological gamblers with healthy controls in both a laboratory setting and in a lounge environment measuring arousal, subjective ratings and heart rate, after gambling on a video lottery terminal. They found that the participants who were in the lounge setting reported higher subjective arousal such as excitement and tension and had a higher heart rate compared to the laboratory setting. This result was independent of what group they belong to (Diskin et al., 2003).

Responses of gambling with regards to gender

The importance of arousal as the explanation for continued gambling has been investigated in a few studies between genders in the gambling literature. Looking at only females Coventry and Constable (1999) showed increased heart rate after playing on a fruit machine in a bingo hall as function of winning but not losing. In line with that study,

examining gender differences, Coventry and Hudson (2001) compared men and women when gambling on a fruit machine in a laboratory setting. Similar to our results in **Paper II** they found no difference in heart rate during gambling between the genders. However, a slight difference was found between a win and a loose, where a smaller increase was seen after a win compared to a loss. This study showed that winning during gambling is needed for increases in heart rate during play (Coventry and Hudson, 2001). Factors, such as stress and anxiety, can also influence heart rate during a gambling session, therefore it is important to note that the findings are not conclusive.

Further, the physiological effects of slot machine play for money or by engaging in the physical activity of pushing buttons and playing, was studied in female problem gamblers and female controls (Meyer et al., 2004, Yucha et al., 2007). It was found that heart rate, respiratory rate and skin conductance increased while playing on a slot machine in both groups of women.

High and low responders

Both animal and humans have shown different response levels to certain substances and situations. These are known as high and low responders. It has been seen that predictive behaviors, for example increased locomotor behavior in animals, in response to different drugs (alcohol, morphine, nicotine, d-amphetamine) indicate that some are high responders (Kabbaj, 2006). In humans high responders, have shown to have an increased cortisol response to stress, have shown a vulnerability to certain types of diseases, for example infectious diseases (Kirschbaum et al., 1995).

High and low responders are further terms used to describe an individuals' varying level of sensitivity to the effects of alcohol. High responders to stress has been found to experience increased subjective

effects of alcohol compared to low responders (Brkic et al., 2016). Stress also plays a direct impact on the subjective effects of alcohol and other substances. Söderpalm and de Wit (2002) discovered that individuals under stress reported an increased level of "liking" towards alcohol compared to control groups without stress. Furthermore, they found that individuals who experienced stress not only consumed increased amounts of alcohol but also consumed more placebo drinks following stress. These results align with previous studies that examined the effects of acute stress on alcohol (Söderpalm and de Wit, 2002, de Wit et al., 2003) and the self-medication hypothesis, which proposes that drug intake increases for relaxation purposes (Swendsen et al., 2000).

High and low frequency gamblers

It is worth exploring how the variations in arousal come about and the potential impact of heightened arousal on persistent gambling. Overall, while there is some evidence to suggest a correlation between gambling frequency and heart rate, further research is needed to fully understand the relationship between the two.

It has been seen that the frequency at which one participates in gambling can impact the subjective response of the individual. Leary and Dickerson (1985) tested the levels of arousal in high and low frequency gamblers. They deemed a high frequency gambler to be someone who played three or more times a week while a low frequency gambler was only playing one time a month or less. Their results demonstrated that while both groups displayed increased arousal, this was more pronounced in the high frequency gamblers (Leary and Dickerson, 1985). This study used measures of arousal that included heart rate and subjective questionnaires not uncommon to our studies in **Paper I and II.**

Moodie and Finnigan (2005) further split the groups between frequent gamblers, non-frequent gamblers and non-gamblers and measured autonomic arousal at a land based casino. They measured heart rate while the three groups played on a fruit machine and found that frequent gamblers had a significant increase in heart rate which also continued after they finished playing. This was not seen in the other two groups. Their study indicated that frequent gamblers are more prone to an autonomic response triggered by fruit machine play (Moodie and Finnigan, 2005).

Further, in a study by Sharpe (1995) high and low frequency social gamblers were compared to non-gamblers. They found that both heart rate and skin conductance was increased after cue induced gambling in all three gambling groups. However, the high gambling group became significantly more aroused than the control groups (Sharpe et al., 1995).

The heightened arousal in response to real-life gambling scenarios appeared to be more significant as shown in some studies (Diskin et al., 2003, Anderson and Brown, 1984). Although laboratory settings may not elicit as strong of a response, physiological reactions can still be observed (Goudriaan et al., 2004, Blanchard et al., 2000, Freidenberg et al., 2002). There is some evidence, however preliminary, that suggest that no difference is seen in the level of physiological arousal between men and women (Coventry and Hudson, 2001). Moreover, there is evidence that indicates a correlation between gambling frequency and heart rate (Moodie and Finnigan, 2005, Leary and Dickerson, 1985).

Neurochemical mechanisms underlying the reward of gambling

Catecholamines have also been found to play an important role in pathological gambling, just as in alcohol addiction. Earlier literature looking at gamblers describes the phenomenon of increased reports of stimulation in circumstances that were associated with gambling (Carroll and Huxley, 1994, Sharpe et al., 1995, Blanchard et al., 2000). There are theories suggesting that gambling problems are influenced by more specifically the neurotransmitter dopamine as it also plays a key role in learning, wanting and craving as well as risk taking (Hing et al., 2016, Robinson and Berridge, 1993). Dopamine is released during pleasurable activities for example exercising, shopping, eating, and sexual activity. It is released in even higher amounts in gambling, as uncertain rewards and 'wanting' are some of the most impactful ways of releasing dopamine. Dopamine is heightened in the moments leading up to a potential reward, the anticipation has been shown to stimulate a 'high' and with repeated exposure to gambling changes occur in the brain that make it harder to resist the temptation to partake and the urge to gamble (Hellberg et al., 2019). Interestingly there is also a dopamine release when we experience a loss while gambling (Barton et al., 2017). This release is higher in people who have gambling disordered as they continue to play even if they have escalating losses. This is often referred to as 'chasing losses'. Gambling disorder individuals believe that their next win could be their next bet (Chen et al., 2022). Once you become addicted it is very hard to stop as the changes within the brain become entrained to the desires of gambling. It has also been suggested that some individuals with altered brain chemistry imbalances; dopamine dysregulation, may potentially be more susceptible to developing gambling disorder (Peters et al., 2020).

This is interesting with regard to the well-known literature in the field of subjective effects of alcohol. In that line of research, it is well

recognized and reported that individual's show differences in the subjective response to alcohol, specifically the feeling of drug-induced stimulation differs among humans. It has been suggested that feelings of positive and stimulant-like effects of alcohol, is related to a much higher level of drug liking and joy inspires the subject to consume more alcohol (de Wit et al., 1987, Chutuape and de Wit, 1994).

Further, increased dopamine metabolites, found in the cerebrospinal fluid, have been seen in pathological gamblers as compared to controls. This result demonstrated a role for dopamine in individuals addicted to gambling (Bergh et al., 1997). Moreover, Meyer (2004) saw important raised levels of dopamine in reaction to casino-gambling in problem gamblers (Meyer et al., 2004). Additionally, research further shows that gambling can cause amphetamine like effects. It has been reported that amphetamine can prime the motivation to gamble and also predict severity of problem gambling (Zack and Poulos, 2004). Furthermore, when looking pre-clinically at rat models, prolonged exposure to a gambling-like schedule of reward by a sucrose solution promoted amphetamine sensitization much like an experience to amphetamine itself (Zack and Poulos, 2004). These studies suggest a dopamine reward similar to those in substance use disorder.

Building on evidence that gamblers show raised dopamine activation in response to gambling, we believe that individuals that show increased sensitivity to the stimulating effects of gambling may engage in higher risks when gambling with money and are therefore more prone to become addicted to gambling.

Pathways into gambling addiction

Gambling is a recreational activity that poses no risk and is a fun activity that incorporates a social element for many people. When looking at pathological gamblers as a group, Blazcynski and Nower

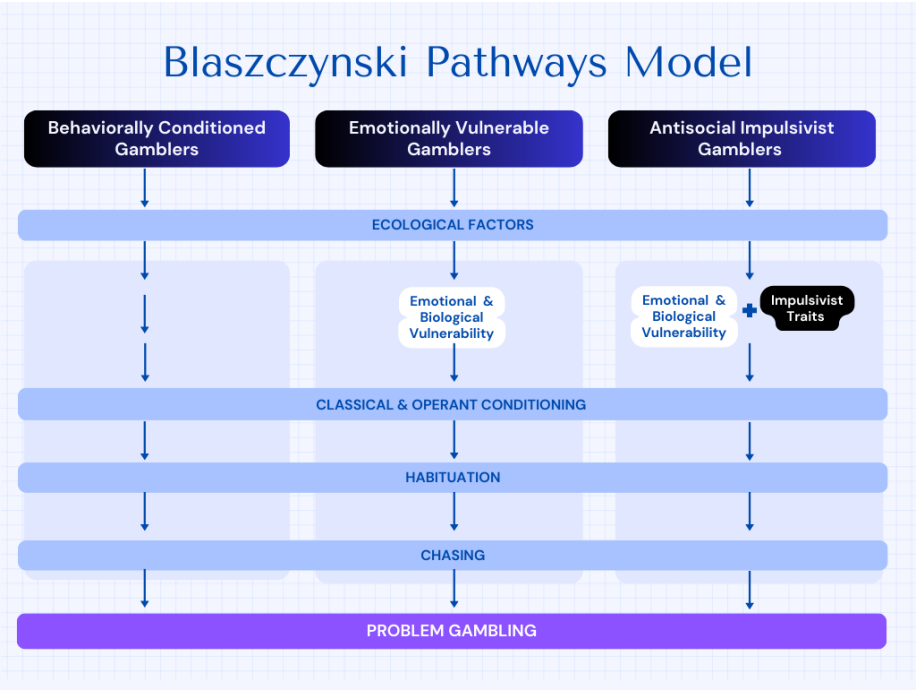
(2002) developed a model that suggests three different pathways into pathological or problematic gambling behavior (Blaszczynski and Nower, 2002). The subgroups of this behavioral model are: the *behaviorally conditioned* problem gambler, the *emotionally vulnerable* problem gambler and the *antisocial-implusivist* problem gambler (Blaszczynski and Nower, 2002).

This model brings into account other contributing factors such as social, psychological and biological components. The first pathway, the *behaviorally conditioned*, is the only pathway that does not include comorbidity, psychiatric conditions, or alcohol abuse as a factor prior to pathological gambling. People fall into this pathway via classical conditioning, and as their gambling escalates, they lose control of their gambling habit which leads to monetary losses and accumulative debt. These consequences are the cause for depression and anxiety from their gambling. They did not start out with these mental health problems before their gambling got out of control. This group has been seen to report well to treatment with limited interventions needed for them to gain control over their gambling disorder.

The other two groups are focused around conditioning and cognitive distortions such as making bad decisions in regards to their gambling habits, which ultimately has led to their gambling disorder. The second pathway the *emotionally vulnerable* has an emotional and biological susceptibility. This group presents with premorbid depression and anxiety, adverse life events and gamble as a form of escapism (Nower et al., 2022). This group is more prone to women who are more likely to start to gamble as a form of relief from their psychiatric comorbid state of depression and anxiety whereas men are more likely to fall into the third pathway which is the *antisocial impulsivists.*

Antisocial impulsivists have a heightened level of impulsivity, they can have substance use problems and antisocial personality traits (Blaszczynski and Nower, 2002, Nower et al., 2022). This third group describes people with psychosocial disturbances caused by their

gambling which carries signs of neurological or disturbed neurochemical dysfunction. It has been seen that gamblers who have a background of impulsivity have a larger range of behavioral problems outside of their gambling. This can include; irritability, suicidality and criminal behavior (Blaszczynski and Nower, 2002).



*Adapted from the Blaszczynski Pathway Model

Treatment seeking men and women

A systemic review analysed the global prevalence of help-seekers for problem gambling and found that only one in 25 ‘moderate risk’ gamblers and one in five people with problem gambling sought help for their problems that were related to gambling disorder (Bijker et al., 2022).

While men still account for the majority of the treatment-seeking population, women are also accounted for and present with a different clinical feature. However, there are limited clinical population studies that measure the differences between genders and most studies predominantly report on the male population, being the dominant representation in this group **Paper III** (Gartner et al., 2022, Mora-Salgueiro et al., 2021).

Women who gamble are typically older, single, live alone, single parents, suffer from a higher level of anxiety and depression and are more likely to be divorced or widowed (Echeburúa et al., 2011, Crisp et al., 2004, Sancho et al., 2019)(**Paper II and Paper III).** Women also progress faster than men into gambling disorder and they also seek treatment at an earlier stage. Women report starting to gamble as a response to psychological stress (Håkansson et al., 2017, Nower et al., 2022). Men when compared to woman tend to live with a partner or be married when seeking treatment for gambling disorder. They have a longer duration of gambling problem before seeking help. Men have been seen to be of the opposite to this and become stressed or depressed due to their gambling habits which is often started off as a hobby or leisure activity while with friends or a social setting (Gartner et al., 2022). However men have been seen to have a higher drug and alcohol use (Echeburúa et al., 2013)**(Paper II and III).**

There is a vast amount of research linking psychiatric comorbidity to gambling disorder. Both alcohol and substance use disorders are well known to be key contributing factors within patients who seek help within the public health care system for gambling disorder (Mora-Salgueiro et al., 2021). Women are predominantly treated for anxiety and depression much more than men, this is where we see women being more incline to fall into the emotionally vulnerable pathway. Interestingly women report to start gambling due to their psychopathology of anxiety and depression and use gambling as an escape. This is in contrast to men who seem to gain these problems as

a consequence of their gambling disorder (Ronzitti et al., 2016, Potenza et al., 2001, Håkansson et al., 2017). Men however are more weighted in the antisocial impulsivist pathway (Blaszczynski and Nower, 2002). Previous epidemiological studies have also reported a high incidence of comorbidity with psychiatric disorders and as well as alcohol and substance use and nicotine among pathological gamblers (Petry et al., 2005, Kessler et al., 2008).

Online casino

Over the last decade there has been a steep increase in access and availability to all types of gambling, especially online casinos and the variety of games available at your fingertips (Gartner et al., 2022). The explosion of new online casinos has catapulted a large number of people globally who are now entrenched within the world of online casino gambling (Håkansson, 2020, Bonnaire, 2012). Online slot machines are one of the most addictive types of games within gambling due to the fast pace and high speed that it allows the player to engage at (Ronzitti et al., 2016). The ease at which anyone can access and use this style of game has become problematic as it is so freely available (Currie et al., 2013, Chóliz, 2016). Near-misses or near-wins are also a contributing factor to the thrill of the slot machine games. Conditional reinforcement is also believed to play a role in contributing to gambling behavior on slot machines, since visual stimuli of flashing lights and imagines add to the enhancement of the gambling experience.

It is further reinforced with music which perpetuates the gambling experience (Pisklak et al., 2020). It has also been reported that people who gambled online had less awareness of their losses when playing online in comparison to those who recreationally gambled using real money on land based casinos (McCormack and Griffiths, 2012). It is strongly believed that money is the motivation for continued gambling

behavior. It could be seen that the uncertainty of the reward could be just as or perhaps even more desirable that the actual win. Uncertainty is a big draw for the player and electronic gaming machines (EGM) are designed to play on our psychological insecurities to hook people in so they continue to spend and play (Delfabbro et al., 2020). This is also the case when looking at gaming for example Candy Crush or Fortnite, these games have been reported as having addictive natures and the levels and winning experience is similar to gambling as you receive prizes that determine moving up to the next level or you can receive more tools to propel yourself further along in the game (Weinstein and Lejoyeux, 2020). Online gaming has also been seen to show characteristics of addiction, such as reward and impulsivity all elements that are linked to the reward system and dopamine release (Weinstein, 2017).

Differences between men and women regarding online casino

Both genders partake in online slot machine play as it is typically one of the most attractive and addictive forms with its fast motions and speed at which it can be played. However, internet gambling in the style of online slot machines has been reported as a preferred form of gambling by the majority of women (Wall et al., 2021). Women report liking more non-strategic types of games like slot machines, bingo, scratch cards and lotto. Men however are more drawn to skill set games like poker or casino games, sports or horse betting (Gartner et al., 2022). It has also been reported that women who actively seek-treatment were more prone to using EGM, for example a slot machine (Kim et al., 2016, Crisp et al., 2004).

AIMS

The overall aim of this thesis was to delve deeper into possible risk factors that may determine the likelihood of a pathway into addictive gambling by exploring the subjective effects. Looking at the differences between gender and the increasing rise of women who are now accounting for the new cases of gambling disorder, as well as exploring the treatment seeking population in Sweden. Further, exploring the subjective effects of alcohol across different age spans to gain insight as to who could potentially be at risk for alcohol use disorder.

Paper I: The purpose of this experimental study was to investigate the subjective and physiological effects of a gambling challenge in both non-gamblers and recreational gamblers.

Paper II: This paper was a post hoc analysis from study one where we divided the groups and examined the data looking at gender. Physiological effects of gambling from a gender perspective and the subjective effects of a gambling challenge from a gender perspective.

Paper III: The purpose of our clinical study was to explore clinical differences in Swedish treatment-seeking men and women with gambling disorder.

Paper IV: This experimental study was to explore the effects of age and gender on subjective responses to alcohol.

METHODOLOGY

Table two details measures used in each method for the individual study.

For a more comprehensive understanding of the materials, methods and laboratory environment used in this thesis, please refer to the individual papers that have been included. These papers provide detailed descriptions of the techniques and materials used for each study. The methods employed in each paper were carefully selected based on the specific research question being asked, they were designed to ensure the reliability and validity of the results that were obtained. By referring to the individual papers, this will provide a more complete understanding of the materials and methods used in this thesis, and this will allow for the findings presented to be more understood at an in-depth level.

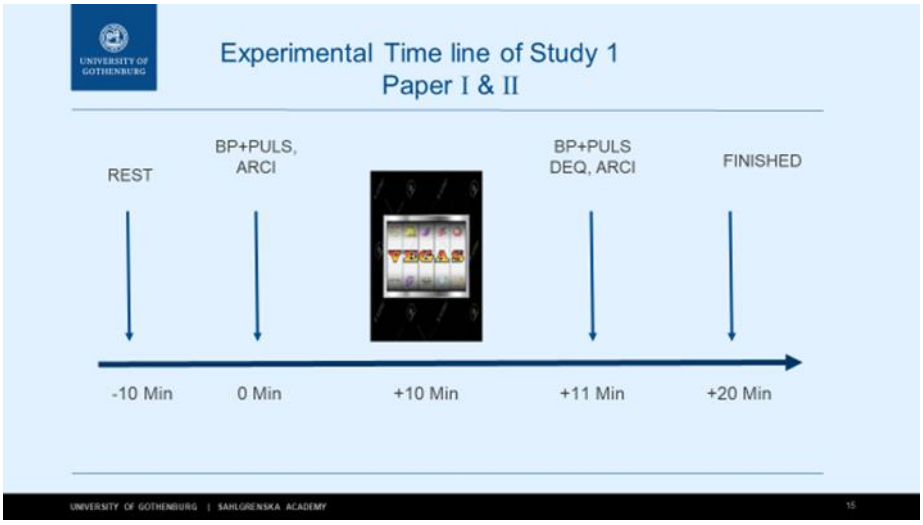
Laboratory Environment (Paper I, II and IV)

The studies were completed in a laboratory setting at Sahlgrenska University hospital in Gothenburg Sweden as part of the Addiction Biology Unit (ABU), Section for Psychiatry and Neurochemistry, Institute of Neuroscience and Physiology. Recruitment for the study was conducted via advertisements placed around busy universities, hospitals, libraries and public places that would gain traction from the general public. The laboratory was set up to mimic a living room setting to achieve the atmosphere of how people would gamble on an online slot machine in the comfort of their own home. The environment also provided at atmosphere for the experience of enjoying an alcoholic drink in the home environment setting. The lounge room at the laboratory was complete with a comfortable sofa, coffee table, armchairs, books and a book shelf, paintings hung on the walls, blankets, coffee and tea making facilities including a kettle and magazines. Participants in the study were asked not to partake in any work, studying, reading or use their phones while in the laboratory. After participants had finished filling in the paperwork that was associated with the study, they were given time to relax and wait for the next stage.

Participants (Paper I and Paper II)

82 participants were recruited for **Paper I and II** (35 men and 47 women) who were recruited via advertisements placed around universities and hospital settings in Gothenburg Sweden. They were initially screened by telephone call to determine whether they met the eligibility requirements.

The inclusion criteria consisted of: age (19–65), normal BMI (18.5–25), moderate consuming of alcohol, (i.e. no more than 9 standard drinks per week for women and 12–14 for men), negative history of substance abuse and or negative history of somatic diseases. Subjects completed the DSM-V diagnoses for gambling addiction (American Psychiatric Association: Diagnostic and Statistical Manual of Mental Disorders) and did not currently receive treatment for gambling addiction. Exclusion criteria are Major Axis I psychiatric disorder (except nicotine dependence), serious medical condition, history of cardiac or liver disease, high blood pressure, history of drug or alcohol dependence (as determined in the diagnostic interview and/or an Audit score over 7), total abstention from alcohol.



The Gambling model

Participants came to our laboratory and were presented with the online casino All JSlots, version 2.2. on a laptop. The slot machine used in the study mimics the exact version that is obtainable online and is complete with all reel features that complete the online gambling casino experience. Online gambling is also accompanied with jackpot wins and losses, flashing sequences and music with line wins, along with brightly coloured imagines. The player has the control to decide how many lines and bets they would like to play.

Clinical patient environment, Study participants and study design

Paper III

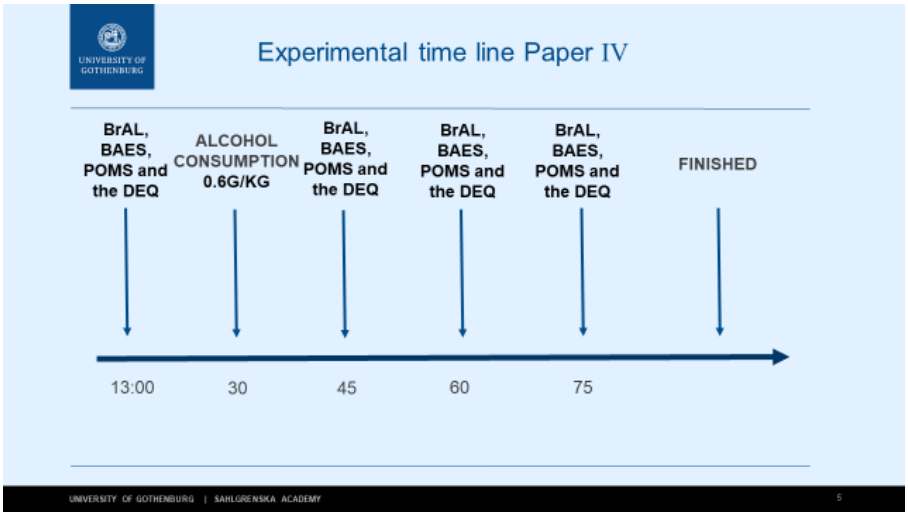
For **Paper III** 204 participants were recruited from a patient group who attended the Clinic for Gambling Addiction and Screen Health at Sahlgrenska University Hospital in Gothenburg, Sweden, the largest public health outpatient facility providing treatment for pathological gambling in Region Västra Götaland in Sweden. The clinic opened in May 2019 and is a clinical setting in a modern environment that is comprised of a comfortable waiting area complete with coffee and tea

making facilities and large treatment rooms where the psychologists treat the patients.

The clinic treats both patients with gambling disorder and gaming disorder from the age of 16 years old. Treatment is based on cognitive behavioral therapy, shown to be one of the most affective in this area of behavioral addiction (An et al., 2017). Patients have the ability to self-referred or be referred by a physician or healthcare professional to the clinic to receive help. There was no explicit inclusion criteria for the clinical study. Patients who came to their first assessment at the clinic were asked if they would like to be included in the study. Patients were not included if they did not meet the criteria for gambling disorder.

Patients that were invited to participate in the study were informed by either a nurse, psychologist or sociologist who were employed at the clinic. Patients were provided all the information and were given instructions to follow at the initial first meeting. Our team of professional staff carefully followed instructions to provide information to all participants that the study is voluntary and they are under no obligation to remain in it if they felt they did not want to continue to participate. They were informed that their treatment would not be affected if they chose to withdraw.

Alcohol challenge: Paper IV



Clinical patient environment, Study participants and study design

Fifty-eight healthy participants (29 man and 29 women) participated in our study and were recruited via advertisements that were placed around Gothenburg, Sweden at public notice boards. Preliminary screening took place over the phone to screen interested participants for eligibility. Participants were required to have a normal BMI (18.5-25), good physical health and a moderate consumption of alcohol. All participants underwent a routine physical examination. Participants filled in the subjective questionnaires prior to their consumption of alcohol then post drinking filled in the subjective measures and DEQ at +15min time points. Blood pressure was also measured at four different time points under the experimental time period.

Table 2. Outcome measures: *Detailed measures used in each method for the individual paper.*

Outcome	Measure	Paper	Reference
DEQ	The Drug Effects Questionnaire (DEQ) is a tool that is widely used in clinical studies. The DEQ consists of four sub-categories: 'effect', 'like', 'high' 'want more'. The DEQ has been used to assess the subjective effects of alcohol and a variety of psychoactive drugs, including stimulants, opioids, and hallucinogens, and has been shown to be a reliable and valid measure of drug effects.	**I, II,** **IV**	(Morean et al., 2013)
ARCI	Addiction Research Centre Inventory is a self-report questionnaire that was developed to measure the subjective effects of psychoactive substances. It has been used to predict the potential for abuse of a substance. The ARCI consists of several subscales, including the Amphetamine (A), Benzedrine (B), Morphine (M), and Lysergic Acid Diethylamide (LSD) subscales, which assess the subjective effects associated with these drug classes.	**I, II**	(Haertzen, 1966, Martin et al., 1971)
Blood Pressure	The DynaMap blood pressure machine is a non-invasive, automated device used to measure blood pressure. It is designed to measure blood pressure using oscillometric technology, which means that it detects the vibrations caused by blood flow in the arteries as the blood pressure cuff is inflated and deflated.	**I, II**	
Structured clinical interview for gambling disorder	Consists of a series of questions and criteria that are based on the diagnostic criteria for gambling disorder. Outlined in the fifth edition of the Diagnostic and Statistical Manual of Mental Disorders (DSM-5). The questions cover various aspects of gambling behavior, such as frequency and duration of gambling, types of games played, amount of money spent, and negative consequences associated with	**III**	(Grant and Potenza, 2004)

	gambling a semi-structured guide for interviewing patients with suspected gambling disorder.		
The Mini-International Neuropsychiatric Interview	A brief structured interview based on diagnostic criteria from the DSM-5 and ICD-10, used to assess the presence of psychiatric disorders. The MINI covers a range of psychiatric disorders, including mood disorders, anxiety disorders, psychotic disorders, substance use disorders, and eating disorders. The interview consists of a series of yes-or-no questions, and the responses are used to determine whether the individual meets the criteria for a specific disorder. The MINI also includes questions about the severity and duration of symptoms, as well as any history of treatment or medication use.	**III**	(Sheehan et al., 1998, Pettersson et al., 2018)
The NORC Diagnostic Screen for gambling problems	A self-report questionnaire measuring the severity of the gambling problem based on the diagnostic criteria in the DSM-5. The NODS consists of 17 questions and assesses a range of gambling-related behaviours, including frequency of gambling, amount of money spent on gambling, and negative consequences associated with gambling. The responses to these questions are used to determine whether the individual meets the criteria for GD. The NODS has been shown to be a reliable and valid instrument for identifying individuals with gambling problems, and the ease of administration make it a useful tool for both clinical and research purposes.	**III**	(Hodgins, 2004, Wickwire et al., 2008)
The Patient Health Questionnaire	It consists of a series of self-report questions that are designed to assess the severity of symptoms over the previous two weeks. These symptoms can include common mental health conditions such as depression, anxiety, and somatic symptoms. The PHQ-9 has nine modules, with each module focusing on a specific mental health condition. The modules include: depression, anxiety, panic disorder, post-traumatic stress disorder, bulimia nervosa, binge eating disorder, somatic symptoms, alcohol use disorder, and suicidal ideation.	**III**	(Kroenke et al., 2001)

	Each module contains a series of questions that are scored from 0 to 3, with 0 representing "not at all" and 3 representing "nearly every day." The scores for each question are added up to obtain a total score for the module. The total scores are then used to categorize the severity of the condition as mild, moderate, or severe.		
Generalized Anxiety Disorder assessment	Generalized Anxiety Disorder (GAD-7) assessment typically involves the use of standardized questionnaires or interviews that are designed to evaluate the severity and frequency of anxiety symptoms. This is also a self-report questionnaire that asks patients to rate the severity of their anxiety symptoms over the previous two weeks on a scale of 0 to 3. Scores range from 0 to 21, with higher scores indicating greater severity of anxiety symptoms. A score of 5 or higher is typically used as a cutoff for further evaluation of GAD.	**III**	(Spitzer et al., 2006)
Gamblers Belief Questionnaire	A self-reported measure that assesses irrational views that gamblers can have around their individual gambling habits. A measure of cognitive distortions in individuals with problematic gambling. It is a 20 item scales in which patients are asked to respond from “strongly agree” to “strongly disagree”. A higher score indicates more irrational thoughts around gambling.	**III**	(Steenbergh et al., 2002)
Alcohol Use Disorder Identification Test (AUDIT)	This test screens for alcohol-related problems and identifies individuals with harmful use of alcohol. It consists of 10 items, separated into three areas: alcohol consumption, symptoms of dependence, and negative consequences of alcohol consumption.	**I, II, III, IV**	(Bergman and Källmén, 2002, Babor et al., 2001)
Drug Use Disorder Identification Test *(DUDIT)*	Known informally as the DUDIT this screening tool is used to determine illicit drug use in individuals. It comprises of 11 questions which determines the severity and frequency of use as well as the negative consequences that are associated with a person’s life.	**III**	(Berman et al., 2005)

Brunnsviken Brief Quality of life scale	Measures an individual's overall quality of life. It is divided into six different life areas such as financial situation, social relationships, overall health, living situation, daily activities and lift satisfaction. Responses are measured on a 7-point Likert scale, where 1 represents "very dissatisfied" and 7 represents "very satisfied."	**III**	(Lindner et al., 2016)
Difficulties In Emotion Regulation Scale	(DERS-16) Measures difficulties in an individual's perception of regulation of their emotions. The scale consists of 16 statements that assess domains of emotion regulation difficulties: no acceptance of emotional responses, difficulties engaging in goal-directed behavior, impulse control difficulties, lack of emotional awareness, limited access to effective emotion regulation strategies, and lack of emotional clarity. Each item is rated on a 5-point Likert scale, where 1 represents "almost never" and 5 represents "almost always."	**III**	(Bjureberg et al., 2016)
The Gambling Pathway Questionnaire	*(GPQ)* The questionnaire comprises 48 statements, and respondents indicate their agreement on a scale of 1 to 6 points (ranging from strongly disagree, 1 point, to strongly agree, 6 points). These 48 responses are categorized into three distinct sub-scales, each representing a particular pathway. The pathways are identified as "behaviorally conditioned gamblers," "emotionally vulnerable gamblers," and "antisocial/impulsivist gamblers."	**III**	(Nower and Blaszczynski, 2017)
The World Health Organization adult ADHD self- reported scale	Is a self-reported scale that is used to assess adult's symptoms of Attention-Deficit/Hyperactivity Disorder commonly known as ADHD. There are six questions related to the symptoms which are impulsivity, hyperactivity and inattention. This is not a diagnostic tool but an assessment of symptoms and points scales to indicate the potential severity if the outcome is indicated higher points scored.	**III**	(Kessler et al., 2005)
The Demographic Data Questionnaire	A data questionnaire collects information about the basic characteristics from a group of people. In these studies the information that was collected was age, gender, race/ethnicity, education level, income, and occupation.	**I, II, III, IV**	

Biphasic Alcohol Effect Scale (BAES)	Self-reported measure used to assess an individual's expectations regarding the effects of alcohol. The BAES includes items that assess positive and negative expectancies, such as feeling more relaxed or outgoing after drinking, as well as feeling sick or losing control.	**IV**	(Martin et al., 1993)
Profile of Mood States (POMS)	Profile of Mood States, which is a self-report measure used to assess an individual's emotional state. The POMS includes items that assess a range of mood states, including tension, depression, anger, vigor, fatigue, and confusion. The POMS is often used in research to assess the effects of various interventions on emotional well-being.	**IV**	(McNair et al., 1971)
The SCL-90	A self-report questionnaire used to measure levels of psychological distress and psychiatric symptoms for an individual. Comprising of 90 items that evaluates a broad range of psychological symptoms, including anxiety, depression, somatization (physical symptoms with no apparent medical cause), and obsessive-compulsive behavior. Participants are asked to rate the degree to which they have felt each symptom over the past week, on a five-point scale ranging from "not at all" to "extremely."	**I, II, III, IV**	(Derogatis et al., 1976)
Breathalyzer	Alcohol breathe tester. Used to estimate the blood alcohol concentration (BAC) in a person's system by measuring the amount of alcohol in their breath.	**IV**	

Statistics:

The statistical analysis for **Paper I and II** was preformed using IBM Statistical Package for Social Sciences software version 25.0 (SPSS, Inc. 2017) and **Paper III** using version 28. The other tests that were done were carried out for **Paper I and II** were using SAS 9.4 (SAS Institute, Inc., Cary, NC). **Paper IV** analyses were performed in SAS® version 9.3 (SAS Institute, Inc., Cary, NC). An in-depth description of the statistical evaluation for each study, can be found in each paper that is presented within this thesis.

Table 3. Statistical methods: Statistical analysis used for each paper that is included in this thesis:

Statistical Method	**Paper I**	**Paper II**	**Paper III**	**Paper IV**
General Linear model (GLM)	X	X		
ANOVA	X	X		
ANCOVA			X	
Shapiro-Wilk test			X	
Chi-square test			X	
Fisher's exact test			X	
Bonferroni test	X	X		
Mann-Whitney test			X	X
t-test			X	
Mixed model analysis				X

Paper I. High Recreational Gamblers Showed an Increased Stimulatory Effects of an acute Laboratory Gambling Challenge

Background: Gambling can be addictive and slot machines are one of the most problematic and popular choices. We explored the subjective and physiological responses to a slot machine in healthy recreational gamblers to identify differences in response among those who gamble recreationally and those who do not, within a laboratory setting.

Method: This study was designed to measure subjective (self-reported questionnaires) and physiological responses (pulse and blood pressure) via a *dynamap* in response to a 10 min gambling task. Eighty-two participants, after meeting the inclusion criteria, were included in the study. They were presented with an online slot machine which mimics the exact style of an online gambling model that is commonly used by people who gamble. Self-report questionnaires of mood and blood pressure were taken before and after gambling.

Results: This study showed that recreational gamblers, and more specifically high recreational gamblers, experienced significantly higher stimulative effects from the online slot machine. This result may be a uniquely predictive behavior for increased risk of gambling.

***Discussion*:** We found that the rewarding feelings achieved from gambling were strong enough to be detected in a laboratory gambling challenge within groups who only gambled around two hours a week. We chose to measure gambling per week in minuets as previous research had measured number of times per week or month. Amount of minutes is a specific and accurate time frame as it demonstrated exactly the amount of time an individual spent on an activity, amount of times played was variable as it did not determine how long each session was played. The findings showed that under laboratory gambling conditions the rewarding effects from a gambling challenge elicited a strong enough response from a group who only participated in gambling activities for money on average for two hours a week. The

drug-like “effect” and “high” was seen in the regular gamblers as well as visual increases on the “want more” and “liking”. When examining the results from the ARCI scale, regular gamblers additionally exhibited a marked increase on the Benzedrine scale when compared to the non-gambling group.

Conclusion: The findings from our study suggest that recreational gambling may have a stimulating effect for certain people. These stimulatory feelings could contribute to the development of problematic gambling behavior for some people. It is however important to note that not everyone in the recreational gambler group experienced this effect, and individual differences in gambling include a variety of reasons that often are driven by a person’s individual, personality and social factors. The role in determining who is more susceptible to these types of effects from gambling, specifically slot machines needs further exploration. Further research within this area will provide a better understanding of the nature of these effects.

Paper II. Subjective and Cardiovascular Challenges to an acute Laboratory Gambling Task in Men and Women

Background: Gender differences in gambling often focus on men being the most dominant. More recently women have been seen to be more represented in new cases however few studies have investigated the subjective and physiological effects from a gender perspective. This paper examined the subjective effects of an acute laboratory gambling challenge between men and women.

Method: **Paper II** was an exploratory post hoc analysis from the data that was collected from **Paper I.** We re-evaluated the data from a gender perspective. Eighty-two men and women (n = 35 men, n = 47 women) were invited to our laboratory and were challenged with an online slot machine for a 10 min gambling session. They completed

self-reported questionnaires to report their mood and subjective responses. Physical measures including blood pressure and pulse were also taken both before and after the gambling challenge in order to identify any physiological changes as a result of the gambling task.

Results: Our findings showed that both men and women equally experienced stimulation when undertaking our gambling challenge. However, men showed an increase in systolic blood pressure in comparison to women, after a gambling challenge.

Discussion: Both women and men equivalently showed stimulatory effects in a laboratory gambling challenge. No gender differences were seen despite previous literature indicating that this would be the predicted result. In this instance gambling was seen to produce an increase of effects in both men and women which indicates the same potential for gambling to be abused. Both groups displayed in increase on the self-reported Drug Effects Questionnaires on all four scales; "effect", "like", "high" and "want". Although the outcome of this paper was in contrast to previous findings, this study indicates the importance of highlighting how both genders are susceptible to problematic gambling behavior as the results indicated that wanting more can be an indicator of potential abuse tendencies. This study was conducted within a group of healthy recreational gamblers who did not have any comorbidities or mental health conditions. The gambling challenge was conducted under laboratory conditions and a different outcome may have been achieved if it were conducted at a land based casino or within a group who were potentially "sensation-seeking".

Conclusion*:* Overall this post hoc analysis provided valuable insight into data that we did not initially consider for a particular analysis or study design. The data should be interpreted with caution and always reported transparently. The outcome of our results showed that both genders equally demonstrated stimulation from our experimental

laboratory study and that both genders are potentially at risk for abuse and the potential harm that gambling may cause.

Paper III. Clinical differences between men and women in a Swedish treatment-seeking population with gambling disorder

***Background*:** The intention of this study was to investigate and evaluate the clinical differences in a group of Swedish treatment-seeking men and women with gambling disorder. It is estimated that 0.2% of women and 0.8% of men have severe gambling disorder. We have seen from previous research and study evaluations that gambling disorder is ever increasing within the female population group. Men are still vastly greater in terms of numbers for gambling disorder, but women are now making up a lot of the new numbers for gambling disorder. In order to understand the clinical differences between the genders, it is important to evaluate the characteristics that differ between the groups. This could potentially determine different treatment pathways if a clearer understanding of how men and women present when seeking treatment.

Method: 204 patients with gambling disorder (26.5% women and 73.5% men) presented at an outpatient clinic in Gothenburg Sweden for treatment of their gambling disorder and were included in our study. They were diagnosed using the SCI-GD and screened for comorbid diagnoses using the MINI. Study patients also completed a range of self-reported questionnaires measuring demographics, gambling disorder, alcohol and other drug problems, symptoms of depression and anxiety, and pathways into gambling problems.

Results: The findings from this study provided valid insight into the the clinical differences between men and women with gambling

disorder in Gothenburg, Sweden. There was a number of different stand out features between men and women who presented to our clinic with gambling disorder. Women were older than men in age and the onset age at which they began gambling. Living conditions for both varied, with women often living alone or being divorced, they also were more likely to have dependent children or be single parents. Men had a longer duration of gambling disorder and began gambling at a younger ager than women. Men were more likely to be married or living with a partner. Men also presented with a higher degree of alcohol and drug use however, women suffered with more anxiety and depression. This was an effect of gambling disorder for men whereas a contributing factor as to why women began to gamble.

Discussion: This study aimed to identify the clinical differences between those who seek treatment here in Sweden and provide a more in depth view of the clinical characteristics which differentiates between the genders. This insight can help to understand the magnitude of instances around the differences as to why people seek help and how they ended up at the clinic for treatment. This in turn could help to provide a better treatment strategy for patient care when looking at the groups from a gender perspective.

Conclusion: This study sheds light on important gender-specific factors that influence the development and maintenance of this disorder. The findings indicate that women with gambling disorder experience higher levels of psychological distress and comorbid conditions, while men are more likely to engage in risk-taking behaviors and experience higher levels of impulsivity. These gender differences have important implications for the assessment, diagnosis, and treatment of gambling disorder, and highlight the need for gender-specific approaches to prevention and intervention. Overall, this study underscores the importance of recognizing the unique clinical profiles of men and women with gambling disorder and developing targeted

interventions that address the specific needs and challenges faced by each gender.

Paper IV. The effects of age and gender on subjective responses to alcohol.

***Background*:** Alcohol is one of the most frequently used substances among aging adults, it may be the most used drug within older adults which could potentially be problematic as the aging process slows down many metabolic pathways leading to miss use with severe consequences. As people age, their bodies may become less efficient at processing alcohol. This means that even small amounts of alcohol can have a greater effect on an older person's body than on a younger person's body. Additionally, certain medications commonly taken by older adults can interact with alcohol, increasing the risk of side effects and complications.

Method: Fifty-eight study participants divided by age in: Younger (18-22 years) middle-aged (38-42 years) and older (58-62 years). Each person was given an alcoholic beverage based on their weight and dosed at 0.6 g/kg alcohol. After consumption a breathalyzer was used to measure alcohol levels and participants were then asked to fill in self-reported measures to report the effects of alcohol. The assessment of the effects of alcohol were assessed across the ascending and descending limbs of the blood alcohol curve.

Results: Study participants in both the older and younger groups both stated increased stimulation when compared to the middle-aged and older participants. Within the younger group, they showed more anger, tension and decreased mood when compared to the middle-aged and older groups. When looking at the groups by gender, it was also seen that men wanted to consume more alcohol in comparison to women and that women displayed a reduced amount of tension and anger.

Discussion: This study demonstrated the difference of subjective effects when looking at an acute dose of alcohol at different age groups. Interestingly there was no difference in breath alcohol levels between the any of the groups irrespective of age. This could be due to what is considered a 'low' dose of alcohol of 0.6g/kg. This study provides interesting results and insight as social alcohol use and alcohol use disorder is a global problem and the importance to understand the subjective effects across the age spans is vital. Gender differences were also identified in this study independent of age.

Both older (58-62) and younger groups (18-22) reported increased stimulation on the BAES scale in comparison to the middle aged group (38-42). The younger group also showed a reduction in tension, mood and anger on the POMS scale in comparison to the middle age and older adults.

Conclusion: It is important for not only older adults to be aware of the potential risks associated with alcohol consumption and to drink in moderation, if at all. Moderate alcohol consumption is generally defined as up to one drink per day for women and up to two drinks per day for men. It is imperative however to note that substance use among aging adults can be particularly dangerous due to changes in the body's ability to process drugs as we age and increased risk of adverse reactions. There is also the potential for interactions with other medications which commonly older adults can be using which may potentially interact with alcohol. Drinking in older adults can be a complex issue. While moderate alcohol consumption has been associated with some health benefits, excessive drinking can lead to serious health problems in older adults.

GENERAL DISCUSSION AND CONCLUSION

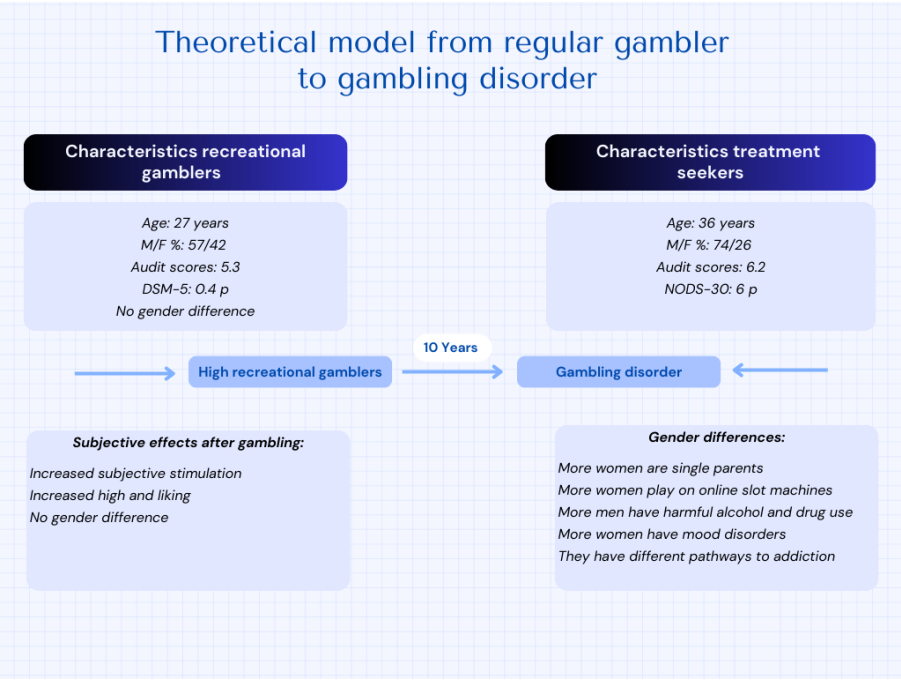
Gambling addiction in Sweden is widespread and includes approximately 134,000 people. That accounts for around 2% of the Swedish population. This equates to approximately 0.6 % of the adult population, with problems that are serious and a further 4% that are in the risk zone for problematic gambling behavior (Socialstyrelsen, 2017). In the Västra Götaland Region (VGR) it is estimated (the calculation is based on the number of applicants to the municipality and user associations in 2016) (Socialstyrelsen, 2017) that there are roughly 3,000 individuals with various forms of risky gambling, from mild conditions to severe addiction.

Despite more research becoming available which in turn increases the understanding of this behavioral disorder, the biological foundations of translating the results into improved prevention and treatment strategies is still a slow process. It is a big task from the health care providers to enhance voluntary take-up of effective safer gambling tools to encourage treatment and care for the populations that requires help within this area. There is a need to re-conceptualize safer gambling habits and to educate and inform the public on these practices. It is important to try to minimize harm for not only those who are not having a problematic gambling problem but to be mindful for all who partake in this risky activity even for recreational purposes.

The principal aim of this thesis was to look at the subjective and physiological effects within a healthy population **(Paper I, II, III and IV)**. We also looked at whether there were gender differences within both social gamblers and social drinkers. We further explored the clinical population who seeks treatment for gambling disorder when looking at the differences between the genders.

There has been limited studies that look at the subjective responses to gambling and even fewer that have examined an individual's response

under laboratory conditions when incorporating what is deemed to be the most addictive form of gambling, a slot machine (Dowling et al., 2005, MacLaren, 2016).



The subjective effects of gambling are complex and vary widely depending on the individual (Brown et al., 2004, Sharpe, 2004). **Paper I** contributes to the knowledge of understanding of the acute experience of a gambling challenge. We found that if you gamble for more than two hours a week you have a greater stimulative response to gambling compared to non-gamblers in the laboratory **(Paper I)**. This means this uniquely predictive behavior is a risk factor for gambling addiction.

Based on previous research looking at gender differences in individuals with gambling disorder, we investigated if there were any differences in the subjective effects between men and women after the gambling challenge in **Paper II** (Potenza et al., 2006, Carneiro et al., 2020).

Interestingly, in contrast to previous research finding strong clinical gender differences (Carneiro et al., 2020, Calado and Griffiths, 2016), we found that both men and women equally experienced a pattern of stimulatory effects after gambling. This highlights and contributes to further knowledge finding that recreational gambling in both men and women seem to have the same abuse potential **(Paper II)**.

Considering the increased prevalence of treatment seeking individuals for gambling disorder in the last ten years, and that women proportionally stands for more new cases with gambling problems or disorders than men (Tavares et al., 2003, Potenza et al., 2001), we made several interesting gender difference observations in our treatment seeking population as seen in **Paper III**. We deepen the understanding and demonstrated that women more often were single parents and suffered from mood disorders compared to men. Men on the other hand suffered more from harmful alcohol and problematic drug use than women did. The men were around five years younger and they had started to gamble ten years earlier than the women **(Paper III)**. These results indicate that mood disorders are a pathway to gambling disorder for women and that a problematic alcohol and drug intake is a risk factor for gambling disorder in men. Healthcare providers for gambling addiction may use these findings to consider specific treatment plans for men and women with gambling disorder.

Alcohol is the most used psychoactive drug in the world (Monteiro, 2011, WHO, 2018). The effect it has on an individual can differ significantly (Li et al., 2020). The individual differences from the effect of alcohol can be due to a number of contributing factors including age, gender, family history of alcoholism, environment and social influence (Verhulst et al., 2015). **Paper IV** revealed that both older and younger subjects reported increased subjective stimulative responses to a moderate dose of alcohol. Young subjects and women also showed decreased tension and anger compared to older subjects and men after alcohol intake. One of the most persistent and significant

problem in the world occurs because of alcohol. Half a million Swedes, both men and women, drink alcohol at high risk levels. 10 000-60 000 drink alcohol at increasing high risk levels for a sustained period of time and will suffer from alcohol-related illnesses or death. These results highlight the importance of understanding how alcohol is experienced during different age spans and gender in social drinkers (WHO, 2018).

Limitations: Subjective effects

Subjective effects measurement questionnaires are commonly used in the field of psychiatry within behavioral research to assess an individuals' experiences, perception, and attitudes in regards to a set of exposed circumstances. When it comes to studying gambling behavior and the subjective effects, these questionnaires have their own set of limitations. Some key limitations to consider when using subjective effects measurement questionnaires for studying gambling include; ***Social Desirability Bias***: participants may provide answers that they perceive as socially desirable or acceptable, rather than their true feelings to the exposure of the experiences. This can lead to inaccurate or biased responses, particularly in a sensitive area such as gambling, gambling behavior and a response to this particular activity.

Limited Insight into Unconscious Processes: Subjective questionnaires primarily capture conscious experiences and perceptions. However, many aspects of gambling behavior, including motivations, decision-making processes, and emotional responses, might also involve unconscious or subconscious factors that are not fully captured by the self-report measures that were applied.

The self-reported questionnaires that were used in study **I, II and IV** are widely used tools that is used to measure the subjective effects of drugs (Moreau et al., 2020). As previously stated, drugs produce feelings of euphoria and “liking”, feelings believed to be connected to if a person choose to take a drug again. These acute responses are

important for continued use. This methodology improves symptom description of gambling and allow a better understanding of the complexity of an individual's gambling behavior.

The scientific methods used today for studying the role of initial and individual subjective responses to drugs in humans are well developed and widely used (de Wit and Phillips, 2012). Laboratory based studies involving drug choice, where controlled doses of drugs are administered and subjective effects are measured, provide us with important information about the relation between drug effects and subsequent use (de Wit et al., 2022). Furthermore, in human laboratory studies, the participant's experience with the drug is less confounded by expectancies or contextual factors. Participants who report experiencing positive drug effects typically choose to consume the drug when given the opportunity.

Yet, in the context of certain drugs it has been noted that subjective drug effects are sometimes difficult to define, and subjective ratings of positive effects such as 'euphoria', 'intoxication', 'high' and 'liking' of a drug may not be readily distinguishable from ratings of apparent negative effects such as 'nausea', 'sick', 'heavy' (de Wit and Phillips, 2012). In addition, initially unpleasant subjective responses to certain drugs may become positive after relatively few uses. These are important limitations that must be brought to attention and new objective methods are needed to further develop research pertaining to the pharmacodynamics actions of drugs of abuse in humans.

These studies differ from previous research on gambling in several ways. First, they advance our understanding of how acute administration of a gambling challenge affects the subjective responses of gambling in humans **(Paper I)**. Subjective effects of both gambling and alcohol are an important factor in drug taking behavior that few laboratories investigate today. Previous studies in humans and in animal research has mostly focused on gambling occasions and on consumption of alcohol. Further pathological gambling has many

comparisons with alcohol addiction in terms of clinical occurrences (e.g. tolerance, loss of impulse control, craving, compulsive use,) and heritability (Hartwell and Ray, 2018). Pathological gamblers also show a comparable stimulation and reward sensitivity while gambling, this is likely mediated by the mesolimbic dopamine system well recognized within the field of alcohol addiction (Bergh et al., 1997).

Second, few researchers, especially in Sweden, explore research on gender difference.

These studies will advance our understanding of how gender affects both gambling and alcohol consumption in humans **(Paper I, II and IV)**. Previous studies are mostly epidemiological investigating how much alcohol people under stress drink and their quality of life (Weera and Gilpin, 2019). Comorbidity and gambling is a primary area of interest with some investigating gender but with little focus on the growing amount of women (Gartner et al., 2022).

Third, several excellent studies have identified events and stimuli that are associated with gender differences and alcohol intake (Erol and Karpyak, 2015, de Wit et al., 2003). Controlled procedures are needed to characterize the time course of vulnerability, including the time course of reactivity to events or stimuli that affect alcohol, and if this differs between men and women.

FUTURE PERSPECTIVES

Future directions investigating the neurochemical mechanisms by which stress may modify both the responses to ethanol or gambling are not known. Stress is a part of normal daily life, and acute stressors are common (e.g., minor accidents domestic or work related disputes, relations at home) and psychoactive drugs such as alcohol are readily available in most people's lives (Powers and Kutash, 1985). There is

evidence to suggest that acute stress increase the propensity to use drugs (Tolic and Soyka, 2018). By unraveling the subjective effects of alcohol and gambling this will improve addiction management and care which in turn will hopefully reduce harm and contribute further to the field of addiction research. Investigating the subjective effects of alcohol and gambling will also advance the understanding, prevention, and treatment approaches. Further studies in this area are much needed and warranted to additionally help to understand the mechanism of the subjective effects within online gambling. The subjective effects within gambling are a potential risk factor that could help us further understand why certain individuals take their gambling to a problematic level. Chasing the stimulatory feelings and feeling high from the effects of playing on a slot machine has from our study been seen to have a similar response to illicit drugs. Looking more at the subjective responses in this area needs a much deeper in-sight to help understand the addictive level of gambling. By continuing to study the underlying stimulatory effects of this addictive behavior it is important to continue to investigate how people respond under different levels of gambling exposure. Previous research has shown that highly stressed individuals are more likely to participate in risk taking activities (Kreek et al., 2005), this needs to be more closely investigated to understand the risks around harmful slot machine and other forms of gambling for these individuals.

People also tend to move between different behaviors in many different incidences, this could be due to fatigue, stress or various life implications. This can determine the choices you make and this has also been seen in gambling behavior (Jauregui et al., 2020). People have been found to be to gambling and problematic gambling at different times and this has the ability to change depending on an individual's state of mind (Sharman et al., 2019). Previous research has shown that for example circadian rhythms are involved in coordination of several neural processes including an impact on behaviors (Pantazopoulos et al., 2018). Circadian rhythm has also

shown that late at night people are more likely to be cognitively loaded, fatigued or in a period of anxiety, under these types of mental fatigue it has been seen that it is more challenging to make difficult decisions and potentially take more risks under these types of conditions as opposed to if they were relaxed or not experiencing stress (Walker et al., 2020, Bishop and Gagne, 2018). During these times they are more likely to make an irrational decision. It is important to identify when in these times of loss of control happens and how to handle the incidences. The shift between recreational gambling and problematic gambling occurs over time and can change under certain conditions, chasing losses or trying to recover debt can be a contributing factor as to how or why gambling progresses into a risky or uncontrolled state of play (Barton et al., 2017). The journey into problem gambling from recreational is one that needs intervention before the problem is reached. Prevention of harm needs much more intervention for all people who engage in all levels of gambling.

A continual monitoring of the treatment seeking population for gambling disorder is of upmost importance. There are limited population group studies and it is important to continue to contribute to this area of research to deepen the understanding of this group. The more knowledge and understanding around the demographics who seek treatment locally as well as globally will help shape future treatment options with a more in-depth understanding around gender and comorbidity. By having a clearer understanding of why, when and how people enter a treatment seeking clinic this will provide a deeper understanding of what the best pathway is for this demographic. It will provide a clearer understanding of what is needed in this area in order to improve care.

An increasing number of studies highlight how important research is around gambling addiction. Limited studies investigate the subjective effects and our studies have shown the link between stimulatory

responses from online slot machine use within a group that recreationally gambles more than low gamblers or non-gamblers.

The interesting finds from our studies included in this thesis highlighted many thought-provoking factors when looking at the subjective effects within online gambling and within alcohol use. By looking at the groups as separate genders it also raised a lot of points that showed what the significant differences are between man and women who recreationally gamble as well as those who seek-treatment for their problematic gambling.

ETHICAL CONSIDERATIONS

Research that includes humans must consider the risks against the rewards of a clinical or an experimental study and considerable ethical considerations have been undertaken in the planning of these studies.

The studies that have been included in this thesis were conformed and conducted in accordance with the declaration of Helsinki. Protocols were approved by the The Swedish Ethical Review Authority. The data is confidential and protected. The subject's name were replaced with a code and only the PI and the technician have the authority to the data code.

All subjects that participated in the studies included in this thesis were *voluntary*. They were free to drop out or withdraw participation at any time throughout the duration of any of the studies, no questions asked. All participants received oral and written information and signed an informed consent form, allowing them to understand the details of the study and outline of the procedure. They were also informed that there was a *confidentiality* agreement protecting their personal data which

remained *anonymous* as well as any events that may occur under the study time. They were also informed of the *potential harm* that may occur. The harm that could potentially be a risk when participants are screened, by filling in their personal information, answering questionnaires such as the AUDIT; DUDIT; SCL90 and the demographics may highlight a potential mood disorder, suicide risk, and drug problems. If they presented reasons that would exclude them from our study or needed to discuss any of the issues that was presented once filling in the questionnaires, the study advisor was there to openly discuss any concerns. They could also be referred to the appropriate medical help facility to assist them if needed.

One of the biggest concerns regarding the gambling challenge was inviting people into our laboratory to *participate in a potentially addictive task*. Online gambling has the tendency for addictive tendencies. We screened all our study participants and part of our exclusion criteria was problematic gambling behavior or alcohol addiction. Previous research has demonstrated that taking a drug in a controlled environment has not been seen to lead to problematic use outside the study. However, with gambling, that is something that is uncertain.

It is also important to consider *results communication*. We informed the participants that they would have access to the published papers. During the study we were as transparent with the results as possible pending that it did not influence the study outcome. For example if the alcohol group wished to know their blood alcohol reading we provided it for them after the trial was completed.

We also believe that participating in these experiments will add to the subjects' knowledge about their gambling habits and alcohol consumption.

However, several ethical factors have been taken into consideration in these studies. This included people with an earlier gambling addiction

were not eligible for **Paper I or II.** The ethics regarding the clinic population in **Paper III** were potential comorbidity risks that are highly associated with disordered gambling.

Paper IV participants were screened with a physical exam which included abdominal palpation, heart rate and blood pressure all performed by a medical doctor. Female participants were also asked to take a pregnancy test prior to drinking alcohol.

As **Paper I** is conducted in a laboratory environment, recreational gamblers participants were observed during the experiment and if any risk would be observed or developed during their time they were with us they receive professional treatment and referrals to the right healthcare were provided.

Paper III included people who attended our clinic in Gothenburg, Sweden to seek help for their already occurring gambling disorder. They were invited to participate in the study and were informed by either a nurse, psychologist or sociologist who were employed at the clinic. Patients were provided all the information and were given instructions to follow at the initial first meeting. Our team of professional staff carefully follow instructions to provide information to all participants that the study is voluntary and they are under no obligation to remain or continue if they felt they did not want to continue to participate. They were informed that their treatment would not be affected if they chose to withdraw.

As the studies for **Papers I**, **II and IV** were conducted in a laboratory environment, recreational gamblers and social drinker participants was observed during the experiment and if any risk would increase or be developed during their time they were with us they receive professional treatment and referrals to the right instance from us.

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