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Neural Correlates of Social Influence Among Cannabis Users

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Abstract

Purpose of review—Although peer influence is an important factor in the initiation and maintenance of cannabis use, few studies have investigated the neural correlates of peer influence among cannabis users. The current review summarizes research on the neuroscience of social influence in cannabis users, with the goal of highlighting gaps in the literature and the need for future research.

Recent findings—Brain regions underlying peer influence may function differently in cannabis users. Compared to non-using controls, regions of the brain underlying reward, such as the striatum, show greater connectivity with frontal regions, and also show hyperactivity when participants are presented with peer information. Other subcortical regions, such as the insula, show hypoactivation during social exclusion in cannabis users, indicating that neural responses to peer interactions may be altered in cannabis users.

Summary—Although neuroscience is increasingly being used to study social behavior, few studies have specifically focused on cannabis use, and therefore it is difficult to draw conclusions about social mechanisms that may differentiate cannabis users and controls. This area of research may be a promising avenue in which to explore a critical factor underlying cannabis use and addiction.

Keywords

Social Influence; exclusion; peer groups; marijuana; cannabis; striatum; insula

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Compliance with Ethics Guidelines

Conflict of Interest

Dr. Jodi Gilman declares that she has no conflicts of interest.

Human and Animal Rights and Informed Consent

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Introduction

Susceptibility to social influence is likely an important risk factor for the development of cannabis use disorders. One of the strongest determinants of both initiation and current use of cannabis is peer networks, particularly for adolescents [1]. Peers play a pivotal role in introducing an individual to a drug [2, 3], and drug use primarily occurs in social settings [4]. Surveys of adolescents [5, 6], college students [3], and treatment-seeking adults [7] consistently find links between peer behavior and drug use. For example, individuals who are more susceptible to peer influence are more likely to have problems with drug and alcohol use, and are more likely to have friends who also engage in risky behavior [8]. Recent studies also suggest that social factors influence treatment and recovery; those with cannabis use disorders who do not seek treatment are more likely to be concerned about the stigma associated with seeking treatment [9, 10**].

It is not surprising that social influence contributes to drug use, as research has consistently shown that the way in which individuals perceive the behavior of others is a strong predictor of their own behavior, especially when the “others” are thought of as a peer group. For example, one study found that college age participants’ alcohol intake is strongly associated with the drinking behavior of their friends, but only loosely associated with the drinking behavior of other students outside their peer group [11]. Similarly, the strongest predictor of an individual’s physical activity is the physical activity of their friends [12]. Peer influence on eating behavior is well-known; individuals eat more when their peers eat more, and eat less when their peers eat less [13, 14]. Peers can also effect delay discounting rates [15], as well as the willingness to expend effort to obtain rewards [16]. However, though a sizable literature exists on mechanisms of influence in the general population, and research supports the notion that social influence can spur drug use and other risky behaviors, there is a wide gap in neuroscience research focusing on substance using populations, especially cannabis users.

The recent upward trend toward greater use of cannabis is an interesting case study for how social mechanisms may influence drug use and dependence. Cannabis is the most commonly used illicit substance among both adolescents and adults in the United States [17], and widespread efforts to legalize cannabis for medical and non-medical use may further increase rates of use. In a recent study surveying young adult cannabis users, nearly half cited social pressure as a motive for using [18]. The current review will focus on the brain regions underlying peer influence during decision-making paradigms, first in the context of social influence, and then in the context of social exclusion. The purpose of the review is to summarize the current research on social influence and cannabis use, with emphasis on the neural circuits underlying of social influence.

Why is Brain Imaging Necessary for Understanding Social Influence?

Investigating neural circuitry of social influence confers important advantages over measuring behavior alone. First, neuroimaging can allow us to test psychological theories about the nature of social influence. Social influence is a subset of social cognition, and refers to the act of changing one’s behavior to match the responses of others. It is important

to note that although social influence often has a negative connotation, more recent studies have characterized peer influence as a socialization process that can facilitate prosocial behaviors in addition to maladaptive risk-taking behaviors [19]. In a broader context, social influence can be thought of as a critical variable influencing decision-making, and can affect a decision at multiple levels. Decision-making consists of specific psychological components, which have been modeled in detail [20–22], composed of five fundamental processes (Fig 1): A. Determining Options, B. Evaluating Options, C. Selecting among Options, D. Decision Processing, and E. Receiving Feedback (from the external and internal environment), which will in turn influence future decisions. Each of these processes can be affected by social influence. Let's take the decision of a teenager to smoke marijuana at a party. First, he will determine his options; he can use marijuana, or he can choose not to use marijuana. These options are largely determined by others at the party. Next, he will evaluate these different options, largely in the context of how he will be perceived by others. He will then select one option; let's say, he decides to smoke. Next, he will experience and process the decision, which will also be largely affected by the people around him. Lastly, he will receive negative or positive feedback regarding his choice, influenced by social factors (e.g., do people look at him strangely? Do more people come up and talk to him?) The feedback will then influence future choices that he makes.

Each of these components of decision-making can be influenced by peers, but there may be significant variation among individuals in how much they are influenced by those around them, and to what extent neural mechanisms are engaged. It is a methodical challenge for researchers to separate out components of decision-making in order to determine at which point social influence exerts its largest effect, and when a social-influence-based intervention could potentially be effective. Using neuroimaging paradigms with event-related designs may help researchers understand each stages of the decision-making process, whereas using behavioral paradigms alone would simply give one output.

Second, a detailed understanding of which brain regions activate during a social influence task can provide clues about what is most salient in the brain when individuals respond to peer influence. For example, during a social influence task, heightened activation of prefrontal regions underlying 'executive function,' would raise a hypothesis that social influence is a factor in evaluating the potential outcome of a decision, whereas heightened activation of striatal regions underlying 'reward' may raise a hypothesis that social conformity is a type of rewarding stimulus, similar to a monetary reward. Therefore, the major advantages of neuroimaging over behavior alone is its potential to determine the "when" and the "where" questions underlying a behavioral output. Characterization of these features of social influence could improve our understanding of a critical behavior underlying cannabis use.

Brain regions Associated with Social Influence

Scientists began studying the neuroscience of social cognition in the 1990's, generally by using functional magnetic resonance imaging (fMRI) while showing participants pictures of social relevance, such as faces, expressions, and the direction of gaze, body posture, and movement. Researchers were able to identify regions of brain activation that were active

during the passive viewing of social information, such as the fusiform gyrus, the superior temporal gyrus and other regions of occipitotemporal cortex (for review, see [23]). These studies, while establishing the idea that certain brain regions are preferentially responsive to social stimuli, generally had participants isolated in the scanner environment, mostly during passive viewing, rather than actively engaging in decision-making processes. Recently, studies have used fMRI to examine more complex social interaction such as social cooperation [24], revenge [25], and the acquisition of social reputations [26]. These studies have established structures in the brain, such as the nucleus accumbens (NAc), caudate, amygdala, cingulate, and anterior insula, that appear to be particularly responsive to these social interactions. These same regions are also associated with social reward and learning, social cognition, and physiological arousal and anxiety, indicating that social interactions, especially conforming or deviating from social norms, generate emotional responses (e.g. [27, 28**, 29]).

Social influence is often associated with heightened neural activation in various regions within what has been called the 'social brain network' [30**, 31, 32]; see [19] for review. This network encompasses regions such as medial prefrontal cortex (mPFC), temporoparietal junction (TPJ), and superior temporal sulcus (STS), and is activated during tasks in which participants are instructed to think about themselves in relation to others (see Fig 2). Many studies also report activity in striatal regions when participants are asked to make judgments involving peer information. In one of the first fMRI studies to directly investigate peer influence, data indicated that the caudate showed heightened activation when participants saw 'popular' compared to 'unpopular' symbols [33]. A second study reported that the NAc, part of the ventral striatum, showed decreased activation when individuals disagreed with peer ratings of facial attractiveness. Furthermore, in this study, deactivation of the NAc during such a conflict with group opinion predicted conformity in future trials [29]. Exposure to social norms can also affect striatal response; a study of young adults reported that the act of agreeing with peers increased activity in the NAc, whereas disagreeing decreased NAc activity [34]. Together, these studies suggest that traditional reward circuitry, such as the caudate and the NAc, may underlie neural processing of consensus or cooperation.

Peer opinion can affect neural response throughout life, but may be particularly salient during adolescence (e.g. [35**, 36, 37, 30]). A study with adolescent participants showed that heightened activation in the striatum and insula, regions involved in affect and reward processing, was associated with peer conflict and with greater risk-taking behavior [38]. Several studies have also shown that simply being observed by peers during risky and non-risky decisionmaking tasks elicited striatal activation in adolescents [39, 40]. In addition, a behavioral study reported a steady decline in social conformity from late childhood through adulthood when individuals rated risky behaviors before and after observing peer ratings of those behaviors [41**]. These studies support the idea that the striatum is sensitive to social context and can be linked to individual differences in sensitivity to peer influence.

Brain regions Associated with Peer influence in Cannabis Users

Neuroscience is increasingly being used to study social behavior (e.g. [23]), but few studies have focused on substance-using individuals, and even fewer specifically among individuals who use cannabis regularly. The primary psychoactive component of cannabis, 9-tetrahydrocannabinol (THC; [42]), binds to the endogenous cannabinoid receptors which are widely dispersed throughout the brain, especially in the cerebellum, prefrontal cortex, cingulate cortex, striatum, amygdala, and hippocampus [43]. Interestingly, many of the regions implicated in cannabis use are also implicated in social behavior (see Fig 2), raising a hypothesis that perhaps cannabis use may alter neural response underlying social behavior.

Existing research, though limited, indicates that activity in the striatum may be markedly altered among those with substance use disorders. In a cohort of healthy adolescents, researchers found that the earlier individuals initiated use of alcohol, cigarettes, and cannabis, the greater the strength of connectivity between reward circuitry (including the striatum) and frontal regions [44**]. This finding is consistent with a large body of research showing that maturational differences in frontal cortical and subcortical monoaminergic systems may underlie impulsivity and/or novelty seeking among adolescents (see [45] for review). Most research into adolescent behavior, however, does not directly address the relationship among peer influence, reward circuitry, and substance use, revealing a fundamental gap in the literature.

A hindrance to our ability to empirically investigate the neural correlates of social influence is a lack of well-validated tasks specifically designed to assess susceptibility to influence. We have attempted to fill this gap with a series of recent studies, in which we adapted classic social psychology task developed in the 1950s by psychologist Solomon Asch. Using a simple paper and pencil line-judgment task, Asch asked participants which line, among three choices, matched the length of another line. Asch demonstrated that individuals were extremely accurate when alone, but when they were with a group of confederates who would give the wrong answer, the majority of participants would repeat the wrong answer. In other words, most participants were likely to agree with peers even at the expense of accuracy [46, 47]. We developed a computerized version of this task that could be performed during fMRI scanning. We developed an initial version of the task, where we showed participants graphs of peer responses to cognitive judgments [48], and then based on the data from this study, made further modifications to the task (including the addition of color photographs of 'peers') [49**] so that we could achieve greater rates of group conformity and better understand how neural activation related to task performance. Conducting these two studies in two different groups of participants had the benefit of allowing us to investigate which findings replicated, which is critical given what researchers have referred to as a "crisis" of replication and reliability in the neuroimaging field [50].

These studies were conducted on young adult (age 18–25) regular cannabis users and age- and gender-matched healthy controls. It is important to note that though there is little consensus in the literature on a standard definition for a 'regular cannabis user', for the purpose of this review, a regular cannabis user is defined as an individual who self-reports using cannabis at least once per week on most weeks. In these studies, participants could

choose whether to follow or oppose group influence regarding which of two lines was longer during a neuroimaging session. We then compared behavior and neural responses between groups. Across both studies, we found that cannabis users and controls were both more likely to follow than oppose group opinions. Only cannabis users, however, showed longer reaction times when going against the group. This reaction time slowing was associated with increased inferior frontal gyrus (IFG) activation, raising the hypothesis that cannabis users compared to controls expended more effortful processing when they opposed group influence. Cognitive variables such as attention and working memory contribute to decision speed, [51, 52] and cannabis use is often associated with these domain-specific deficits [53–55]. The longer reaction time during the trials in which the cannabis users disagreed with the group may have indicated that the cannabis users had less ability to identify and/or resolve information conflicts (though this interpretation is one among many, and should be verified in future studies). In addition to reaction time differences, we also found significant differences between cannabis users and controls in neural activation, specifically within social influence trials. In these studies, cannabis users, but not controls, showed bilateral caudate activation when exposed to social information. We hypothesized that hyperactivation of the caudate in cannabis users indicated this group, relative to controls, showed greater responsiveness in the reward regions of the brain when presented with social information. We note that in this study, heightened activation in the caudate was specific to the social influence component of the task, and not to the monetary feedback, indicating that perhaps hyperactivation of the caudate was specific to peer influence and not an overall hyper-reactivity to reward, though this needs to be replicated in larger samples.

The caudate is not only important for social decision-making, but may be sensitive to individual differences in susceptibility to influence. Across groups, activation of the caudate correlated with self-reported peer conformity. In other words, activation of the caudate was particularly heightened in those who valued group conformity. Previous studies have suggested that the mesocorticolimbic circuitry underlying reward largely overlaps with valuation of social stimuli [56, 29]. Social conformity is likely incorporated with other standard reinforcement parameters (e.g., effort, reward magnitude, probability) to derive a subjective value for a given option [57]. Greater activation of mesocorticolimbic circuitry in the cannabisusing group may indicate that this group may place a higher value on social conformity relative to controls. It is important to note that several studies have reported differences between cannabis users and controls in structure [58, 59] and function [60–62] of mesocorticolimbic circuitry, especially the ventral striatum/nucleus accumbens complex. Both the ventral and dorsal striatum, including the caudate and putamen, play a prominent role in decisionmaking, and are likely affected by cannabis use due to the high density of cannabinoid receptors throughout this region (see [63] for review). The striatum, particularly the caudate, is also implicated in habit formation, a process by which over time (in the transition from casual drug use to addiction), drug-taking becomes controlled largely by automatic rather than deliberative processes [64].

Brain regions Associated with Social Exclusion in Cannabis Users

Ostracism, or social exclusion, causes significant distress, and even sends neural signals of pain. Individuals who use cannabis may not only show greater sensitivity to social

information, but may also be more sensitive to social exclusion. Anecdotally, individuals often report that desire to avoid social rejection underlies their use of drugs in social settings. The relationship between peer groups and drug use, however, is complex. On one hand, people tend to use cannabis primarily in social settings [4]. On the other hand, youth who are isolated from their peers are more likely to use tobacco than those who are integrated into peer groups [65, 66]. Indeed, one study found that adolescents who were isolated, but peripheral to substance-using peer groups, had an increased likelihood of substance use [67], suggesting that social isolation may increase vulnerability to substance use for youth connected to substance-using peers.

As with social influence, few studies exist that investigate the neural circuitry of social exclusion in cannabis users. We conducted such a study in cannabis users by scanning individuals during a task called Cyberball, an interactive computerized ball-toss game [68] in which individuals are included, and then subsequently excluded, from the game. A recent meta-analysis of the Cyberball paradigm [69] identified a set of critical brain regions involved in the processing social exclusion, including the right insula, the ventral anterior cingulate cortex (vACC), and the dorsal anterior cingulate cortex (dACC). Results from our study showed that although cannabis users and controls reported similar levels of distress from social exclusion, the cannabis group showed significantly less activation than controls in the right anterior insula during peer rejection. This is intriguing, given that insula activation to social exclusion was the most highly replicated finding in the meta-analysis of Cyberball paradigms. The anterior insula is involved in many brain functions such as subjective awareness [70] and cognitive control [70, 71], and is associated with experiences of physical pain [69, 70] and processing of negative emotions [72, 73]. The anterior insula has also been implicated in drug craving [74–77]. There are several interpretations of what reduced insula activation in cannabis users may reflect, but one plausible hypothesis that that cannabis users show impaired processing of social information. In fact, a study of adolescents using Cyberball showed that more socially competent adolescents showed greater activity in the insula, suggesting that heightened interpersonal skills may be associated with increased neural sensitivity to peer rejection [36]. Reduced insula activity during peer rejection could also indicate that cannabis users were less conscious of social norms. Insula activation may underlie an ability to reflect on social situations, and this ability may produce greater sensitivity to peer relationships [78]. Additionally, cannabis use has been associated with anhedonia, (e.g. [79]), indicating that emotional response may be dulled in the cannabis group.

Though cannabis users had reduced insula activation, they showed normative processing in the vACC. Like the insula, vACC activation has been reported in studies of emotion, especially sadness [80–82]. However, unlike the insula, the vACC has been more specifically associated with affective conflict during cognitive tasks [81]. A recent study reported increased connectivity between vACC and default mode network (DMN) regions during social exclusion [83], suggesting that during exclusion blocks, when the participant is perhaps ruminating on the situation, they may be engaged in reflective processing. DMN functional connectivity to vACC is stronger in people with depression compared to controls, suggesting an association between vACC-DMN connectivity, negative emotion, and rumination [83, 84]. Activity in the vACC during social exclusion likely reflects not only

negative emotion produced by social exclusion, but also affective monitoring, which may be intact in the cannabis group. It is also plausible that vACC dysfunction may become apparent in heavier users, or in those with cannabis dependence. Further studies are needed to better understand the factors contributing to altered insula response, but possibly in fact vACC response, within cannabis users.

Limitations of Current Studies and Future Directions

Though there is increasing focus on neuroscience underlying influence, there is a clear need for more of this research to focus on substance using populations, especially cannabis users. Studies in cannabis users indicate that brain regions such as the caudate, insula, and prefrontal regions, may show altered activation during the processing of social information. The studies reviewed, however, are cross-sectional, and therefore we cannot draw conclusions about causality. Longitudinal studies are needed in order to determine whether altered neural response to social influence/exclusion is a risk factor for cannabis use, a consequence of cannabis use, or a combination of both. Without such longitudinal studies, there are several possible explanations for these differences; 1) altered neural response is a trait that reflects a pre-existing risk for initiation of cannabis use, 2) altered neural response developed as a result of cannabis exposure due to disruption to neurodevelopmental processes underlying social processing, 3) a third variable is responsible for giving rise to both cannabis use and altered neural responses to social cognition, such as striatal reactivity, or 4) some combination of the explanations above is responsible for of the relationship between cannabis use and altered neural responses.

Understanding which mechanism is responsible for the differences observed in social processing may lead us to identifying who is at risk for cannabis use disorders, and help us to develop treatments that can target this risk. Neuroimaging may allow us to better understand at what point in the decision-making process cannabis users diverge from controls, and to form hypothesis about how brain regions underlying these differences map onto motivations for cannabis use. Clever task designs can also help us better disentangle which aspects of social decision-making differ (e.g. social reward vs general reward). Brain regions implicated in social processes, in cannabis use, and in both are depicted in Fig 2; further research is needed to fully understand interactions and networks that may differ in cannabis users.

It is important to note that in many of the social influence and peer rejection studies described above, brain differences often occurred in the absence of behavioral differences (for commentary, see [85]). It is important to acknowledge that scanner-based experimental psychology tasks represent simplified traces of complex real-life behaviors. Our tasks, like most neuroimaging tasks, investigated decision-making during low-arousal tasks where the outcomes (comparing the relative length of lines, being excluded from a ball-tossing game) are not particularly meaningful or salient. Social influences that occur in the context of drug use are likely to be high-arousal, personally meaningful, and require complex balancing of costs and benefits. Future studies can employ tasks more relevant to drug-seeking and drug-using behavior, to further probe whether more effortful tasks would reveal behavioral

differences as well better understand the predictive utility of slowed decision making in understanding real-world functional outcomes.

Furthermore, it is important to note that although peer influence often has a negative connotation, more recent studies have characterized peer influence as a socialization process that can facilitate prosocial behaviors in addition to maladaptive risk-taking behaviors [19]. For example, the presence of peers during late adolescence has been linked to more exploratory behavior, as well as higher learning rates [86]. Therefore, future research into social mechanisms of cannabis use should take into consideration the positive aspects of peer influence.

Finally, cannabis users with heavier patterns of use (dose, quantity, frequency, and duration of use) are subjected to greater adverse impacts of cannabis on brain structure and function (e.g. [87**]). Therefore, future studies should compare heavy (e.g. daily) to non-heavy (e.g. weekly) users, as well as current heavy users to past heavy users, in order to investigate whether neural response to social information varies as a function of cannabis exposure over time. Furthermore, young adults using other substances such as alcohol or nicotine may also show differences in brain-based activity to peer influence. An additional avenue for research is to examine how different motivations for drug use (e.g. coping, social engagement, etc.) contribute to different patterns of brain activity underlying social influence and drug use. Finally, a myriad of other factors (e.g. age of onset of cannabis use, gender, comorbid psychopathology, educational attainment) should also be taken into account when considering how social cognition interacts with cannabis. In addition, age likely plays a prominent role in the mechanisms underlying social influence, as many studies have shown that regions underlying reward, such as the ventral striatum, is heightened in adolescents during risk decision-making [39] and during social interaction tasks [40]. It will therefore be critical to study the neuroscience of peer influence in cannabis users with a wide age range.

Conclusions

The neuroscience of social influence in cannabis users is in its infancy, and future research needs to be conducted to better understand the role of social influence in initiation and maintenance of cannabis use. The limited literature identifies structures such as the striatum and insula as possible biomarkers for altered social cognition, which raises hypotheses that can be tested in future studies. Larger populations of cannabis users, such as individuals of different ages and different cannabis use trajectories, should be furthered studied, as social influence may prove to be an important predictor of the development of, and recovery from, cannabis use disorders.

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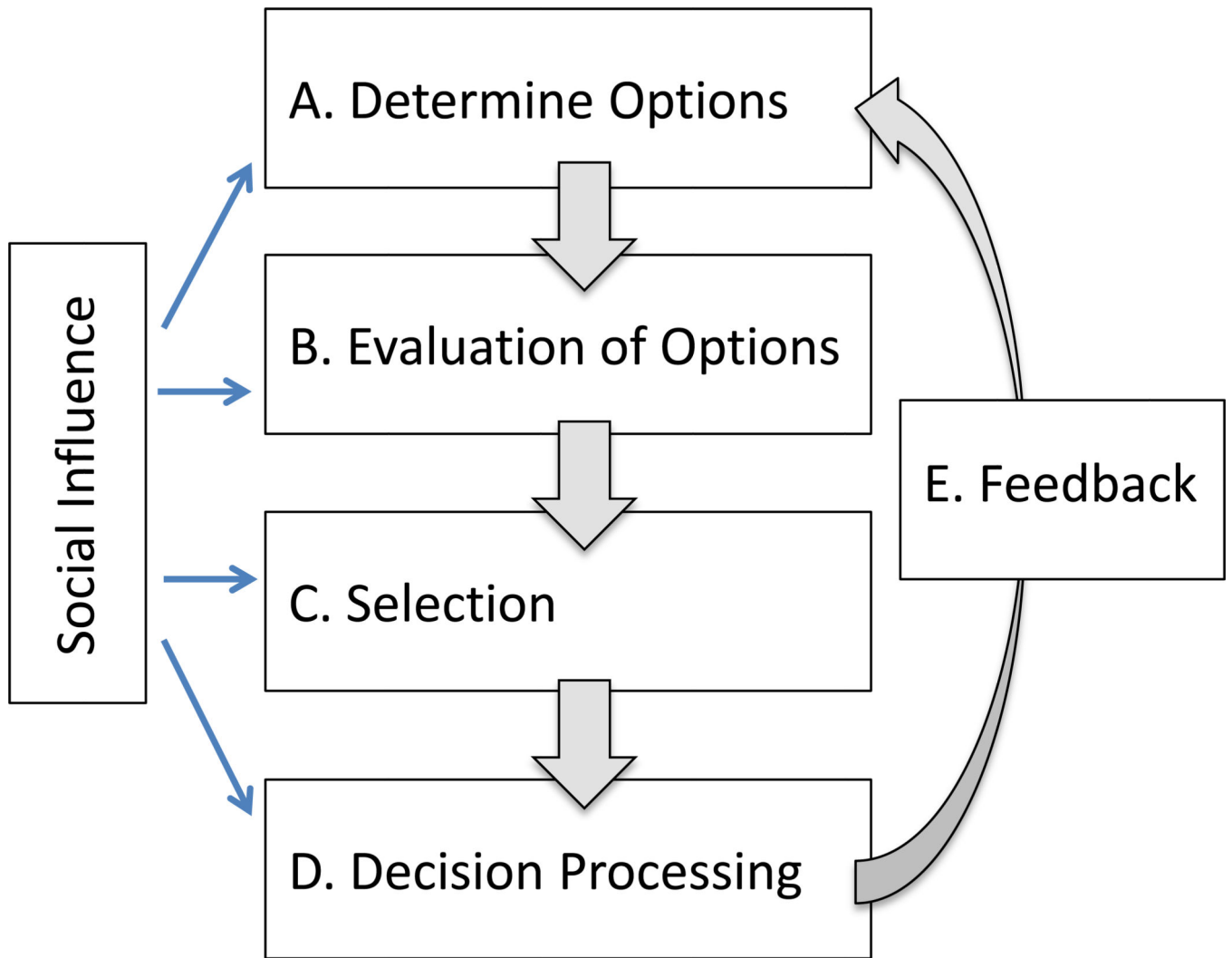


Figure 1. Heuristic model of decision-making. This schematic outlines a set of processes that occur during decision-making, each of which can be affected by social influence.

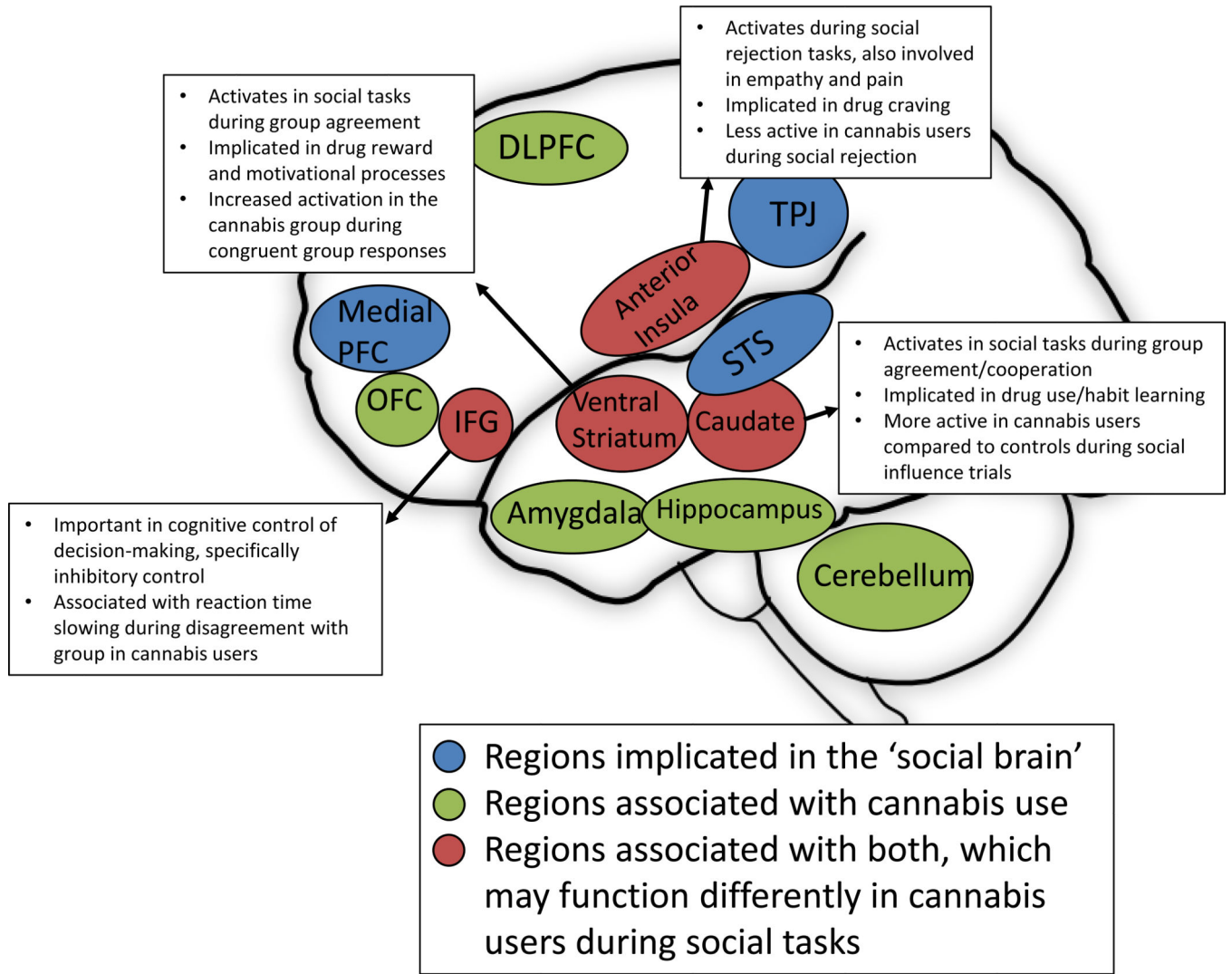


Figure 2. Brain structures involved in social cognition (shown in blue), cannabis use (shown in green), and with both social cognition and cannabis use (shown in red). This figure emphasizes structures discussed in this review, but is likely incomplete, as future studies may show other structures/networks that are important in social cognition and are impacted by cannabis use.