The neural correlates of reinforcement sensitivity theory: A systematic review of the (f)MRI literature.

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Abstract

Objectives

Reinforcement Sensitivity Theory (RST) is a theory of motivation, emotion and learning, that has been translated into an account of personality. RST proposes neural structures that form the basis of systems responsible for reward (BAS), punishment (FFFS) and conflict processing (BIS). This systematic review collated studies examining psychometric measures of RST alongside structural and function MRI data to (i) examine how psychometric RST is associated with the proposed neural topologies of RST, (ii) identify any common associations between psychometric RST and other brain regions, and (iii) provide recommendations for advancing the current literature base.

Methods

Initial search terms identified 10952 papers. After processing, 39 papers that investigated the association between RST scales and neural functioning in healthy adult samples were included in this review.

Results

There was general support for associations between the BAS and the structure/activity of the pre-frontal cortex and ventral striatum with some additional findings for the ventral pallidum and ventral tegmental area. There was also some support for associations between BIS/FFFS and structure/activity of frontal regions, cingulate cortices and the amygdala.

Conclusions

Overall, psychometric correlates of RST were associated with activity in proposed neural circuitry, with the most consistent support being found for the BAS; however, psychometric and experimental limitations still hamper the differentiation of the BIS and FFFS systems in their activation of deeper brain networks. Future studies need to include revised RST scales that separate the BIS and FFFS and implement more rigorous tasks that allow for the examination of each system both independently and codependently.

Keywords: Reinforcement sensitivity theory, Magnetic resonance imaging, systematic review

Public Significance Statement

This paper examined the neural correlates of reinforcement sensitivity theory (RST) by systematically reviewing (f)MRI literature that compared findings with a psychometric measure of RST. Findings generally support the neural structures laid out by RST for the behavioral activation system and there was some support for the behavioral inhibition system and fight-flight-freeze system. Future research needs to address the issues identified by this review, mainly the reluctance to use a psychometric scale that encapsulates revisions to the theory.

1 Introduction

1.1 Reinforcement Sensitivity Theory

Reinforcement sensitivity theory (RST), first posited by Jeffery Gray in 1982, is a neurobiological account of motivation, emotion and learning, that has been subsequently translated into an account of personality (Smillie, Pickering & Jackson, 2008). Based on animal research, RST was initially concerned with examining anxiety and classifying the underlying brain systems involved. After evidence indicating that the functioning of these systems varied between individuals in a stable manner, a theory of personality based on motivation and emotion was born (Gray & McNaughton, 2000). The original theory (Gray, 1982) proposed 2 neurobiological systems: the behavioral approach system (BAS) modulating appetitive motivation and the behavioral inhibition system (BIS) modulating aversive motivation. The BAS was sensitive to conditioned reward and related to trait impulsivity. The BIS was sensitive to conditioned aversive and high intensity stimuli and associated with trait anxiety.

By the late 1990's a wealth of research emerged that indicated that fear and anxiety were distinct processes. Firstly, animal studies found that defensive behaviours could be divided and differentiated by orientation to the threat, with one division of behaviours orientated to cautiously approaching threat and the other division orientated to escaping the threat (Blanchard & Blanchard, 1990a, 1990b). This division was further supported by studies finding anxiolytics affected defensive behaviours orientated towards threat while not affecting those orientated away from threat, whereas the opposite was found for panicolytics (Blanchard, Griebel, & Blanchard, 2001; Blanchard, Griebel, Henrie & Blanchard, 1997; Griebel, Blanchard, Jung, Masuda, & Blanchard, 1995). Based on these divisions in defensive behaviours, RST was substantially revised (Gray & McNaughton, 2000).

As the BAS is not a defensive system it remained largely unchanged (although it is now responsible for processing all appetitive stimuli, not just conditioned), however, the role of the BIS changed significantly with the addition of the flight-fight-freeze system (FFFS), which is now responsible for processing all aversive stimuli (conditioned and unconditioned), behaviourally represented by defensive/active avoidance behaviours and emotionally expressed as fear (McNaughton & Corr, 2004). The BIS is now proposed to be a mediating system for approach-avoidance conflicts between BAS and FFFS activation (though also for approach-approach or avoidance-avoidance conflicts). Its output is characterized by behavioural inhibition to allow for conflict monitoring and increased risk assessment, behaviourally expressed as defensive approach/passive avoidance behaviour and emotionally reflected in anxiety responses (McNaughton & Corr, 2004). Alongside proposing the behavioural and emotional functioning of these systems, RST outlines the neural structures and pathways that physically underpin these systems. The proposed neural topology of each system will be discussed, starting with the BAS and moving on to the hierarchically organised BIS and FFFS. Psychometric measurement of RST will be discussed, followed by the aims of this review.

1.2 The Behavioral Approach System

The BAS is proposed to be located in neural structures that are responsible for processing reward - namely the dopaminergic system consisting of the ventral tegmental area (VTA), ventral palidum (VPal), ventral striatum (VS) and prefrontal cortex (PFC; Gray & McNaughton, 2000). Together, these structures form the majority of the mesocorticolimbic dopamine system, also referred to as the reward system (Arias-Carrión et al., 2010; Haber, 2011). The first component, the VTA, is one of the main dopaminergic structures in the brain, alongside the

substantia nigra (Trutti, Mulder, Hommel & Forstmann, 2019), though due to their proximity, imaging studies struggle to precisely differentiate these two structures (Trutti, Mulder, Hommel & Forstmann, 2019). The VTA has two dopaminergic pathways: The mesolimbic pathway connects the VTA to the nucleus accumbens (NAcc), which is the primary structure of the VS. The mesocortical pathway connects the VTA to frontal areas, predominantly to the dorsolateral PFC (dlPFC). These dopamine pathways fire in response to both primary and conditioned reward (Pickering & Smillie, 2008) and play a significant role in reward motivation, processing, and learning (Haber & Knutson, 2010; Pickering & Gray, 2001).

The VPal is located below the striatum and has connections within the reward system to the VTA and VS, as well as projections outside to the limbic system (see Haber & Knutson, 2010 for review). It has been found to play a role in processing a wide range of rewards, such as food, sex, and money (Smith, Tindell, Aldridge & Berridge, 2009), and is proposed to code hedonic and motivational salience, with suggestions that it may be the final pathway for reward (Smith, Tindell, Aldridge & Berridge, 2009).

The VS is mainly comprised of the NAcc but is still loosely defined in humans and may contain parts of the caudate and putamen that are generally considered as part of the dorsal striatum (see Haber & Knutson, 2010 for review). The NAcc receives inputs from a wide array of areas ranging from the PFC to the brain stem and outputs to the VTA and VPal, as well as the hypothalamus and bed nucleus of the stria terminalis (Haber & Knutson, 2010). Striatal activity increases during processing of both primary (e.g., consumption of food) and secondary (e.g., monetary gain) rewards (O'Doherty, Buchanan, Seymour & Dolan, 2006; Breiter, Aharon, Kahneman, Dale & Shizgal, 2001; Knutson, Adams, Fong & Hommer, 2001).

The final structure of the proposed BAS circuitry is the PFC, which has a range of sub areas involved in reward processing. Firstly, the dorsolateral PFC is the gateway for the mesocortical dopamine pathway, it modulates reward processing in the striatum (Staudinger, Erk & Walter, 2011), and cognitive processes necessary for reward processing (e.g., allocation of attentional resources; Wallis & Kennerley, 2010). The orbitofrontal cortex (OFC) is involved in guiding decision making, alongside the ventromedial PFC (vmPFC) that plays a role in determining expected value of potential rewards and evaluating received reward (Peters & Büchel, 2010; Rushworth, Noonan, Boorman, Walton & Behrens, 2011; Wallis & Kennerley, 2010). Although RST initially proposed the BAS to be located in this 4-structure (VTA, VS, VPal, PFC) network, recent work has proposed the need for the integration of the BAS with the wider body of research on the reward system (Krupic & Corr, 2017). This could incorporate the hippocampus (implicated in reward memory; Lansik, Goltstein, Lankelma, McNaughton & Pennartz, 2009) and amygdala (implicated in reward prediction, learning and reward related arousal; Baxter & Murray, 2002; Murray, 2007) into the structural anatomy of the BAS.

1.3 The Fight Flight Freeze System

The BIS and FFFS are both neurologically organized in a hierarchal structure based on the proximity of the threatening stimulus, called *defensive distance*, but differ in the orientation to the stimulus referred to as *defensive direction* (McNaughton & Corr, 2004). The FFFS has a defensive direction that is orientated away from the potential threat (active avoidance). According to McNaughton & Corr (2004), at the most proximal *defensive distance*, where the most intense active avoidance response is seen, activity is predominately located in the periaqueductal gray (PAG). As defensive distance increases, the pattern of activity shifts to

higher level regions, moving first to the medial hypothalamus, followed by the amygdala, anterior cingulate cortex (ACC) and finally the prefrontal ventral stream at the largest (safest) defensive distance. The PAG is seen as one of the more primal core brain areas (Motta, Carobrez & Canteras, 2017), whose stimulation is related to fight, flight, and freeze behaviours (Assareh, Sarrami, Carrive & McNally, 2016; Deng, Zhao & Wang, 2016). The PAG projects to the medial hypothalamus, which is involved in encoding and retrieving fear memories, as well as responding to threatening stimuli (Gross & Canteras, 2012). In response to threatening stimuli, the hypothalamus acts as a go-between for information passing between the PAG and amygdala, however, it is skipped in response to painful stimuli (Gross & Canteras, 2012; Motta, Goto, Gouveia, Baldo, Canteras & Swanson, 2009). Although often seen as a purely fear related structure, it has also been implicated in processing of primal rewards, suggesting that different distinct areas may be involved in multiple motivation systems (Motta, Carobrez & Canteras, 2017).

The amygdala has long been seen as the central hub for fear processing (Davis, 1992). It has been implicated in fear learning (Kiefer, Hurt, Ressler & Marver, 2015) and organization of immediate and more long-term threat responses (Davis, Walker, Miles & Grillon, 2010). The amygdala mediates threat response through intra-amygdala circuits and projections to other fear circuitry such as the hypothalamus and PAG (Gross & Canteras, 2012; Fox & Shackman, 2019). The ACC has been implicated as a key structure in contextual fear memory and modulating fear expression, which are firmly in the remit of the FFFS (Frankland, Bontempi, Kaczmarek & Silva, 2004; Tang, Ko, Ding, Qiu, Calejesan & Zhuo, 2005; Einarsson & Nader, 2012; Milad, Quirk, Pitman, Orr, Fischl & Rauch, 2007). However, the dorsal ACC has been identified as a

potential conflict monitoring system, which suggests different subregions of the ACC may be attributed to either the BIS or FFFS (Botvinick, Cohen & Carter, 2004).

RST proposes that activity in the prefrontal ventral stream is related to the most complex forms of defensive avoidance at the most maximal defensive distances. Behaviours such as stereotyping (Milne & Grafnam, 2001; Quadflieg et al., 2009), obsession (Apergis-Schoute et al., 2018; Fineberg et al., 2018) and responses to small monetary loss (O'Doherty et al., 2001) can be reflected in the neural activity in the prefrontal ventral stream. However, a review of ventromedial PFC functioning has found it to also be responsible for processing rewards suggesting it is not purely an avoidance-based structure (Oldham et al., 2018). That said, it was stated in the revisions that it does not imply that these areas are solely devoted to defense, just that they are involved in response to distal threat (McNaughton & Corr, 2004).

1.4 The Behavioral Inhibition System

The defensive direction of the BIS is orientated towards the threatening stimuli (passive avoidance behaviour). At the most proximal defensive distance the main areas of activity are the amygdala and septo-hippocampal system. As defensive distance increases to safer levels activity patterns shift to the posterior cingulate cortex (PCC) and finally the prefrontal dorsal stream (Pickering & Corr, 2008). The septo-hippocampal system (SHS), containing the septum and hippocampus, is the key network implicated in the BIS (Gray, 1982). The area was identified in anxiolytic drug studies that found similar effects to hippocampal lesions on animal anxiety behaviours (Gray, 1982). RST proposes that SHS is involved in cognitive aspects of more conventional anxiety and generalized anxiety disorder (McNaughton, 1997), but encodes all types of anxiety (McNaughton & Gray, 2000). The hippocampus has long been accepted as a key structure in cognitive processes, such as memory and learning (Teyler & DiScenna, 1985;

Eichenbaum, 2017; Bird, 2017). This functioning makes it a critical structure within the BIS, due to the mediating role it plays. Indeed, hippocampal dysfunction has been found to impair extinction of avoidance learning, which may lead to persistent avoidance responses seen in anxiety disorders (Cominski, Jiao, Catuzzi, Stewart & Pang, 2014). The revised version of RST, in particular highlights the role of the amygdala in processing both fear and anxiety (LeDoux, 1994; McNaughton & Corr, 2004). More specifically, with regard to BIS, the amygdala is responsible for controlling the level of arousal (McNaughton & Gray, 2000). Sole activation of the amygdala would be characterized as a pure fear response, but simultaneous activation of the SHS and amygdala constitutes an anxiety response (McNaughton & Gray, 2000).

As threat becomes more distal it is proposed activity moves to the PCC. The PCC has been implicated in memory retrieval, planning and controlling attentional focus (Leech & Sharp, 2014). In the RST context, the PCC is proposed to be related to higher order anxieties that lack any simple avoidance strategies, such as agoraphobia or nyctophobia (Corr & McNaughton, 2004). The attribution of the PCC to the BIS is supported by reviews indicating its role in the assessment of potential threat (Fiddick, 2011), a key aspect of the BIS.

At the most distal defensive distances activity is located in the prefrontal dorsal stream. It is proposed that the prefrontal dorsal stream controls high level passive avoidance and risk assessment behaviours and is related to deep forms of obsession and complex forms of anxiety, such as social anxiety (Corr & McNaughton, 2004). Indeed, this is supported by studies finding decreased regional homeogenity in the dlPFC of individuals with social anxiety disorder (Qui et al, 2011). The dlPFC has also been found to influence activity in other brain areas in response to predictable threat, while the dorsomedial PFC (dmPFC) influences activity when processing unpredictable threat (Wheelock, Sreenivasan, Wood, Ver Hoef, Deshpande & Knight, 2014).

1.5 Psychometric evaluation of RST

Although RST started as a bottom-up neurobiological theory of personality, the most widely used method to quantify individual differences in the subsystems of RST is the use of psychometrics (Smillie, 2008). There are currently two streams of psychometric evaluation for RST; scales developed on the basis of the original theory and more recent scales developed considering the revisions to RST. The most widely used original scales are the BIS/BAS scale (Carver & White, 1994) and the Sensitivity to Reward/Sensitivity to Punishment questionnaire (SRSPQ; Tourrubia, Avila, Moltó & Caseras, 2001). These scales were designed to quantify the two systems of the original RST, and thus, do not separate the BIS and FFFS, though attempts have been made to distinguish the systems from items in the BIS/BAS scale (Heym, Ferguson & Lawrence, 2008), which may prove useful in uniting findings from studies that examined original RST with the theoretical changes seen in revised RST. Nevertheless, these original scales are still being widely used since the revisions to RST to classify approach/avoidance tendencies (e.g., Balconi, Angioletti, De Filippis & Bossola, 2019; Sun, Luo, Chang, Zhang, Liu, Jiang & Xi, 2020; Bossola, Angioletti, Di Stasio, Vulpio, De Filippis & Balconi, 2020). More recent scales have been designed based on the revised RST, such as the RST-PQ (Corr & Cooper, 2016), RSQ (Smederevac, Mitrović, Čolović & Nikolašević, 2014), rRST-Q (Reuter, Cooper, Smillie, Markett & Montag, 2015) and the Jackson 5 (Jackson, 2009). Each of these scales separates the BIS and FFFS, allowing for a more theoretically sound measure of RST. However, issues remain in fully encapsulating all RST aspects (see Corr, 2016; Krupić, Corr, Ručević, Križanić & Gračanin, 2016; Walker & Jackson, 2017). The revised scales should be more useful in delineating structures that have distinct and shared roles in different RST systems. For example, the PAG is attributed to the FFFS and has been implicated in instinctual emotional

processes such as defensive responses and fear learning but it also plays a role mediating reward seeking behaviour and goal-oriented responses to more primal rewards such as food, water and drugs which suggests it may be involved in the BAS in some form (see Motta, Carobrez & Canteras, 2017).

1.6 Neuroimaging techniques

There is now a wealth of neuroimaging techniques available to study the brain; from electroencephalogram (EEG) which offers superb temporal resolution (Gui et al., 2010), to Computed Tomography (CT) scans that offer a more structural view of the brain (Jeena & Kumar, 2013). One of the most widely used neuroimaging technique is Magnetic Resonance Imaging (MRI) and functional MRI (fMRI; Glover, 2011). MRI uses gradients in magnetic fields to create images of the brain with great spatial resolution, however, is only useful for examining structure rather than functioning (Glover, 2011). This was overcome by the development of fMRI, which can image regional, time varying changes in the brain by assessing metabolic changes, which are reflective regional activity (Glover, 2011). FMRI offers great spatial resolution but can also offer temporal resolution in the 100ms range (Ogawa et al., 2000). This technique's ability to offer great temporal and spatial resolution makes it an informative tool to examine the proposed neural structures of RST systems and will be the focus of this review.

1.7 Aims & Objectives

The current systematic review has three aims. Firstly, it aims to investigate the relationship between psychometric measures of RST and the theoretically proposed neural circuitry of RST. For both the original and revised psychometrics to be considered as valid measures of individual differences in reinforcement sensitivity, they must be associated with the

neurological systems put forward by the RST. In other words, the scales should be able to discern individual differences in the structure, activation, and connectivity of the proposed systems. Secondly, it aims to identify other areas outside of the proposed neural circuitry of RST that may need to be incorporated into the theoretical framework of reinforcement sensitivity. Finally, it aims to provide recommendations for future studies that examine the neural correlates of RST – in terms of methodological considerations and theoretical implications.

2. Method

2.1: Research Strategies

The literature search was conducted in four international electronic databases: Scopus, PsychInfo, Web of Science and PubMed. From this cohort only peer-reviewed full-text journal articles written or published in English were included. The research was restricted to studies conducted on healthy adult samples with no restrictions regarding gender or ethnicity. The search terms aimed to capture all studies that used certain forms of neuroimaging (MRI, fMRI, EEG, MEG) alongside a psychometric evaluation of either original or revised RST. The search was conducted in November 2019. The search of the database was conducted using the following search terms:

"Reinforcement Sensitivity" OR "Behavioural Activation" OR "Behavioural Approach" OR "Behavioural Inhibition" OR ("fight" AND "flight") OR "BAS" OR "BIS" OR "FFFS" OR "FFS" OR "Punishment Sensitivity" OR "Reward Sensitivity" AND "neural" OR "biobehavioural" OR "neuropsychology" OR "neuroimaging" OR "Magnetic resonance imaging" OR "MRI" OR "functional magnetic resonance imaging" OR "FMRI" OR

"Electroencephalography" OR "Event Related Potentials" OR "Event-Related Potentials" OR "ERP" OR "magnetoencephalography" OR "MEG".

An updated search was performed in April 2021 to account for studies that had been published between 2019-2021 and to account for the initial use of the English spelling of "behavioural" instead of the more widely used American spelling of "behavioral". This search found 20042 studies which was reduced to 5338 studies after duplicate removal and accounting for the results of the original search. This led to the inclusion of 3 extra fMRI-based studies that were published after the initial search. There were no additional studies found due to changing the search terms to American spelling.

2.2: Eligibility Criteria

The results of the systematic review were examined by two researchers (first and second authors - both PhD students). Results were first checked for duplicates, with any duplicates being removed. Title and Abstracts were then scanned for inclusion based on the following criteria: (i) Contained a neuroimaging technique (e.g., MRI, fMRI, EEG), which led to the exclusion of studies that may have discussed neural structures but did not directly use neuroimaging; (ii) Included a psychometric assessment based on RST (e.g., BIS/BAS, RST-PQ, SRSPQ), which led to the exclusion of studies using only potentially related psychometric scales (e.g., impulsivity, extraversion, neuroticism), but not those that included at least one direct measure of RST; (iii) Explicitly examined RST in relation to the neuroimaging data, which led to the exclusion of studies that have collected neuroimaging data and psychometric data, but did not directly compare them; (iv) Contained a healthy adult sample, which led to the exclusion of studies on

adolescents and individuals with various disorders (e.g., alcohol disorder); (v) The papers were available in English language format, which may have led to the exclusion of relevant papers that were not available in English.

The exclusion of studies based on title and abstract were completed independently by both researchers, and subsequently included papers were compared and discussed to make sure no relevant papers were omitted. After the researchers reached agreement of inclusion of research, the body of research was split into two separate reviews - the current on research investigating MRI and fMRI, and a second one on investigation into research investigating EEG and ERPs (Firth, Standen, Sumich & Heym, 2022). Each researcher performed an in-depth examination of the content of their relevant research and excluded any papers that did not meet the eligibility criteria. Data were then extracted, with each researcher reviewing a subsample of the other's papers to maintain consistency and correct procedure. Therefore, the current study focuses on relevant MRI (structural and functional) literature only.

2.3: Quality assessment

The 20-item AXIS assessment tool was used as part of quality assessment (Downes, Brennan, Williams, & Dean, 2016). Each study was assessed individually and assessed a score out of 20. The AXIS rates the papers on a wide number of factors related to methods, sample, and reporting. Previous research has used cutoff points of 0-7 for low quality papers, 8-15 for medium quality papers and 15+ for high quality papers (Wallace, Heym, Sumich & Fido, 2020). All studies in this review were deemed as high-quality papers based off their AXIS score being greater than 15.

2.4: Data selection

Table 1 shows all the data included in this review.

Table 1: *Details of studies included in the systematic review*

***** Insert Table 1 about here******

3: Results

3.1: Study selection

The below PRISMA flow chart provides an accurate summary of the articles identified, screened, and finally included in this paper (Figure 1; Moher, Liberati, Tetzlaff, Altman & The PRISMA group, 2009). It also breaks down the split of studies for the current MRI systematic review and its sister EEG systematic review (Firth, Standen, Sumich & Heym, 2022).

******Insert Figure 1 here**********************************

Figure 1: PRISMA flow chart of selection process

3.2: Structural studies looking at grey matter volume (GMV)

Seven studies examined GMV, with 5 studies using the SRSPQ (Tourrubia, Avila, Moltó & Caseras, 2001) and 2 using the BIS/BAS scales (Carver & White, 1994) to assess RST. Of the studies using the SRSPQ, 2 studies found a positive correlation between sensitivity to punishment (SP) and GMV in the right hippocampus (Barros-Loscertales et al., 2006a; Levita et al., 2014) with the study looking at an all-male sample finding also positive correlations with GMV in the parahippocampus and amygdala (Barros-Loscertales et al., 2006a). One other study supported the positive correlation between SP and GMV in the amygdala in males, but not females (Adrian-Ventura et al., 2019). Three studies investigated sensitivity to reward (SR). One

study, using an all-male sample, found a negative correlation with GMV in the caudate, putamen, superior frontal cortex and globus pallidus (Barros-Loscertales et al., 2006a). Another study also found a negative correlation between SR and GMV in the left caudate (Parcet et al., 2020). The final study that investigated SR found a negative correlation with GMV in the ACC, the medial and left lateral PFC, left and superior temporal lobe and the left insula for both genders, and in the NAcc and left caudate for males only (Adrian-Ventura et al., 2019b). Of the studies using the BIS/BAS scales, BIS was found to be positively correlated with GMV in the hippocampus in one study (Cherbun et al., 2008). The other study found BIS to be negatively correlated with GMV in the parahippocampus and BAS to be positively correlated with GMV in the vmPFC and inferior parietal lobe for females, but an exactly opposite pattern for males (Li et al., 2014).

3.3: Resting state connectivity and other resting state studies

Three studies investigated BAS-related traits and resting state connectivity. One study found a positive correlation between SR and ACC-vmPFC and vmPFC-VTA connectivity (Adrian-Ventura et al., 2019). One study found a positive correlation between BAS and left-right striatum and right frontal gyrus-right striatum connectivity (Dong et al., 2018). One study found a positive correlation between BAS-Fun Seeking and OFC-putamen connectivity and a negative correlation between BAS-Drive and middle cingulate cortex-caudate connectivity (Angelides et al., 2017).

Four studies looked at other resting state measures. A positive correlation was found between SR and the hurst component in the VS and OFC (Hahn et al., 2012). A negative correlation was found between SP and regional homogeneity in the amygdala and hippocampus (Hahn et al., 2013). A positive correlation was found between BAS-Fun Seeking and fractional anisotropy in the left corona radiata and superior longitudinal fasciculus and with diffusivity in the left inferior

longitudinal fasciculus and the inferior fronto-occipital fasciculus (Xu et al., 2012). Finally, a negative correlation between BIS and the number of white matter fibres in corpus callosum , the fibre density in the unicate fasciculus and the number of fibres in the right and left accumbofrontal tracts (Park et al., 2021).

3.4: Monetary incentive-based tasks

Twelve studies used monetary incentives in their tasks. Of these, 8 studies included an examination of brain activation during a monetary incentive delay (MID) task in relation to RST Four studies found a positive correlation between SR scores and activity in the VS during reward processing (Costomero et al., 2013a; Hahn et al., 2009; Hahn et al., 2011), and the BAS scale (Simon et al., 2010). This was further supported by three studies using other money-based tasks, with two finding a positive correlation between the BAS scale and activity in the VS while processing reward (Dong et al., 2018; Eryilmaz et al., 2017), and one specifically for the BAS-Drive subscale (Customero et al., 2016). A positive correlation was found between activity in the medial OFC and SR (Hahn et al., 2009) and BAS scores (Simon et al., 2010) when processing rewards. One study found a positive relationship between SR and activity in the left midbrain when processing reward (Costomero et al., 2013a). One study found a negative correlation between SR and midbrain-OFC connectivity during incentive processing and SR and NAcc-left amygdala connectivity during reward anticipation (Costomero et al., 2013a). A positive correlation between SR and activity in the DMN and right FPN during anticipation of rewards and punishments (Costumero et al., 2015). Finally, one study found a positive correlation between SR and activity in both the PCC and precuneus in men when comparing dollar wins to no win (Dingra et al., 2021).

Regarding BIS/FFFS traits, SP was found to be positively correlated with amygdala-hippocampus connectivity during loss anticipation by 2 studies (Hahn et al., 2010; Hahn et al., 2013). However, the 45 participants used in the 2010 study were also used in the 89 participant study from 2013, which may explain the repeated findings. One study found and a negative correlation between BIS and activity in the VS when receiving reward (Simon et al., 2010). Another study found a negative correlation between SP and activity in the right middle frontal and postcentral gyri for women when comparing dollar wins to no win conditions as well as a negative correlation between SP and activity in the right anterior insula, left superior frontal gyrus and right temporal gyrus for women only (Dingra et al., 2021).

3.5: Affective picture-based tasks

Six studies investigated the relationship between RST and brain activity when viewing affective pictures. For BAS traits, a positive correlation was found between SR and activity in frontal areas such as the OFC (Customero et al., 2013b) and the medial PFC (Barros-Loscertales et al., 2010), but negatively with activity in the superior frontal gyrus when viewing erotic images (Barros-Loscertales et al., 2010). Positive correlations were also found for SR and activity in the right occipital gyrus, precuneus (Barros-Loscertales et al., 2010), the left insula and left VS (Customero et al., 2013b) when viewing erotic images. BAS was found to have a positive correlation with activity in the left hippocampus/parahippocampus (Reuter et al., 2004) and with modulation of the FPN, but a negative correlation with modulation of the DMN when viewing erotic images (Costumero et al., 2015). One other study looked at positive valence and found a significant difference between high and low BAS groups, with high BAS individuals showing greater activation in the middle cingulate cortex, right NAcc, right precuneus, superior orbital/medial gyrus and middle temporal gyrus (Radke et al., 2016). One study found SR was

found to be negatively correlated with activity in the right lateral PFC and left occipital cortex when viewing aversive images (Barros-Loscertales et al., 2010).

Only one study looked at BIS in relation to erotic images and found a positive correlation with the activity in the left ACC, thalamus, right amygdala, insula, left basal ganglia, left brain stem & PCC, with a negative correlation with activity in the right OFC (Reuter et al., 2004). A positive correlation was found between BIS and activity in the ACC, PCC and thalamus for fear evoking and disgusting stimuli, as well as a positive correlation with activity in the amygdala for fear evoking images (Reuter et al., 2004). Finally, one study split groups into high and low BIS conditions and found greater activation in the dlPFC to angry faces and greater activation of the right dorsal ACC to fearful faces for the high BIS condition (Bunford et al., 2017).

3.6: Food related tasks

Four studies used food related tasks. Van Rijn et al., (2016) examined the association between RST and neural activity in the sating of hunger. They found that for those in the hunger condition, activity in the VS (specifically the caudate), amygdala and ACC correlated negatively with BAS-Drive when receiving calories. For those in the sated condition BAS-Drive was positively correlated with activity in the left caudate. One study found a positive correlation between BAS-Drive and activity in the left OFC, right VS amygdala, VTA and VPal and between BAS-Reward responsiveness and activity in the OFC and VPal when viewing appetizing food images compared to bland food images. They also found a positive correlation between BAS-Drive and activity in right OFC and right VS when viewing disgusting food images compared to bland (Beaver et al., 2006). One food related study used sweets as a reward in a card guessing game with high and low rewards and losses (Luking et al., 2013). BAS was positively correlated with activity in the inferior frontal gyrus in low loss trials, and with activity

in the right caudate and the right lateral OFC when comparing low loss trials to neutral trials. However, these same regions were negatively correlated with BAS when comparing higher loss to lower loss trials. Neseliler et al., (2017) examined neural responses to high and low-calorie food during exam and non-exam periods. They found BIS was negatively correlated with connectivity between the vmPFC and dlPFC but positively correlated with activity in the vmPFC and amygdala when comparing the exam condition to the non-exam condition for high-calorie images compared to low-calorie images.

3.7: Go/No-Go tasks

Two studies investigated the association neural responses to Go/No-Go tasks and the SR scale of the SRSPQ (Funetas-Claramonte et al., 2016a; Funetas-Claramonte et al. 2016b). The first study found SR correlated with increased activity in the inferior frontal gyrus for No-Go and infrequent Go trials compared to frequent Go trials (Funetas-Claramonte et al., 2016a). The second study used a stop signal variation of the Go/No-Go task (Funetas-Claramonte et al., 2016b), showing a negative correlation between SR and the left fronto-parietal network and the anterior DMN for stop error trials. SR also had a positive correlation with activity in a cluster containing the bilateral precentral and postcentral gyri, the superior parietal cortex, the bilateral supplementary motor area, and the right cerebellum in stop error trials. SR had a negative correlation with the midline network (containing the ACC and supplementary motor area, the bilateral middle and superior frontal gyri, the bilateral inferior parietal cortex, including the supramarginal gyrus, and the bilateral insula) for successful stop trials.

3.8: N back tasks

Two studies looked at neural responses to an N back task using the BIS/BAS scale. The first study used a 3 back task while pre-exposing the participants to pleasant, unpleasant, and neutral videos (Gray & Braver, 2002). BAS was negatively correlated with activity in the caudal ACC and the posterior rostral ACC for the average of all affective states. When broken down into affective states, BAS was negatively correlated with activity in the caudal ACC for all emotions and BIS was positively correlated with activity in the caudal ACC for pleasant stimuli. When controlling for task related activity in the neutral condition, BIS was positively correlated with activity in the caudal ACC for pleasant stimuli, BAS was negatively correlated with caudal ACC activity in the unpleasant condition. Gray et al. (2005) built on this study by examining a wider array of brain areas on a larger participant pool. They only looked at neutral affective states in their analysis. They found that BAS was negatively correlated with item-related activity in the dorsal ACC, the bilateral PFC, and the bilateral parietal cortex. BAS was positively correlated with state-related activity in the right parietal cortex. BIS was positively correlated with state-related activity in the rostral ACC.

3.9: Switching tasks

Two studies investigated task switching paradigms using the SR subscale of the SRSPQ. In an all-male sample, Avila et al., (2012) found a positive correlation between SR scores and set switching neural activation in the right VS and right inferior frontal cortex, and a negative correlation between SR and activation in the rostral ACC. Funetas-Claramonte et al., (2015) found a negative relationship between SR and neural activity in the inferior frontal gyrus, dlPFC, the ACC, the inferior parietal cortex and postcentral gyrus, and a positive relationship between SR and activity in the posterior cingulate cortex in switch versus repeat contrasts. They also found a negative relationship between left VS activity and SR during switch cues.

3.10: Priming tasks

Two tasks investigated neural activity in response to priming tasks. Mortensen et al., (2015) looked at an all-female sample using a combination of the SRSPQ and neuroticism scales to target all three RST systems. They used SR for BAS, SP for the FFFS and neuroticism for BIS. SR scores were positively associated with activity in the left posterior hippocampus and parahippocampal gyrus for all contrasts, but only in the left caudate nucleus and NAcc in response to valid and invalid targets, in the right OFC and left thalamus in response to cues and valid targets, and in the right caudate nucleus in response to cue primes only. They then used SR scores adjusted by either SP (SR/SP) or N (SR/N) scores to examine the joint subsystems hypothesis. SR/SP and SR/N with activity in the left VS, bilateral OFC and left thalamus for all contrasts. For SR/SP, peak activity was located anterolaterally in the caudate and spread into the NAcc and putamen, and correlated with activity in the left posterior hippocampus, parahippocampal gyrus, fusiform cortex, right lateral occipital cortex and left opercular cortex. SR/N activity peaked posteromedially in the VS, spreading only to the NAcc, and was also associated with activity in the bilateral inferior temporal gyrus, left middle temporal gyrus, right inferior and middle frontal gyrus, and the bilateral OFC. Examining left VS activity, SR was positively, whereas SP and N were negatively correlated. Straumen et al., (2012) found no association between BIS/BAS scale and neural activity in response to a priming task that masked words from participants' prevention and promotion goals.

4. Discussion

4.1: The proposed neural structure of the BAS

RST proposes the BAS is located in a dopaminergic system consisting of the PFC, VS, VPal and VTA (Gray & McNaughton, 2000). This review has found psychometric measures of BAS to be associated with activity in the PFC (Barros-Loscertales et al., 2010; Funetas-Claramonte et al., 2015; Gray et al., 2005), and more specifically the OFC (Hahn et al., 2009; Simon et al., 2010; Customero et al., 2013a; Customero et al., 2013b; Luking et al., 2013; Mortensen et al., 2015). There was also some evidence of structural and resting state differences in the PFC in relation to BAS trait measures (Adrian-Ventura et al., 2019b; Hahn et al., 2012; Li et al., 2014). The involvement of the VS as a BAS structure was consistently supported by correlations with task related activity (Customero et al., 2013a; Customero et al., 2013b; Customero et al., 2016; Hahn et al., 2009; Hahn et al., 2011; Simon et al., 2010; Dong et al., 2018; Eryilmaz et al., 2017; Radke et al., 2016; Van Rijn et al., 2016; Mortensen et al., 2015) and structural and resting state differences (Adrian-Ventura et al., 2019b; Hahn et al., 2012; Barros-Loscertales et al., 2006a; Parcet et al., 2020). BAS was also found to be related to connectivity between the right and left striatum and right frontal gyrus and right striatum (Dong et al., 2018). However, there were limited of findings in regards to the VPal and VTA. One study found a relationship between BAS-Drive and activity in the VTA and VPal and BAS-reward responsiveness and activity in the VPal (Beaver et al., 2006). Another study found a relationship between BAS and GMV of the nearby structure, the globus pallidus (Barros-Loscertales et al., 2006a). The VTA was also found to be related to BAS traits in terms of its connectivity to the vmPFC (Adrian-Ventura et al., 2019ba). Although there was relatively little support for an association between trait BAS and the VPal and VTA, they are critical in reward processing and motivation (Smith, Tindell, Aldridge & Berridge, 2008; Haber & Knutson 2010) and are undoubtedly part of the neural make-up of the reward system. As the BAS is fundamentally a reward processing system it

seems unlikely that the VTA and VPal are not part of the system. It may be that the BAS psychometrics do not effectively isolate the individual differences in the sensitivities of these systems or the tasks do not adequately activate each processing stage of the BAS.

4.2: The proposed neural structure of the BIS and FFFS

This review only found studies that used measures of the original RST, though one study tried to account for a 3-system hypothesis by using a neuroticism measure as index for BIS in addition to the SPSRQ as proposed indices for FFFS and BAS (Mortensen et al., 2015). Therefore, BIS and FFFS have to be evaluated here together rather than as separate structures. At maximal defensive distances, RST proposes BIS activity is located in the prefrontal dorsal stream and FFFS is located in the prefrontal ventral stream (Corr & McNaughton, 2004). This is partially supported by findings that BIS was related to greater activation of the dlPFC when viewing angry faces (Bunford et al, 2017), and in the vmPFC when viewing high calorie food images in addition to reduced dlPFC-vmPFC connectivity (Neseliler et al., 2017). As defensive distance shortens BIS activity moves to the PCC and FFFS activity moves to the ACC (Corr & McNaughton, 2004). Accordingly, both the PCC and ACC were related to BIS when viewing disgusting and fear evoking images (Reuter et al., 2004), and latter also when processing fearful faces (Bunford et al., 2017), performing a standard N back task (Gray et al., 2005) and an N back task after watching a pleasant video (Gray & Braver, 2002). Although it was expected that ACC activity would be associated with BIS/FFFS it is surprising that this is seen in response to pleasant stimuli; however, the authors were cautious about interpreting these findings due to power issues (Gray & Braver, 2002).

In line with the proposition of the septohippocampal system as the main system underpinning the BIS, hippocampal structure was associated with BIS measures (Barros-Loscertales et al., 2006a;

Cherbun et al., 2008; Li et al., 2014; Hahn et al., 2013); however, this was not seen for hippocampal functioning. In terms of the involvement of the amygdala, original BIS trait measures were associated with task related activity (Hahn et al., 2010; Hahn et al., 2013; Reuter et al., 2014), resting state measures and structure of the amygdala (Adrian-Ventura et al., 2019b; Barros-Loscertales et al., 2006a; Hahn et al., 2013). For BIS specifically, the amygdala is proposed to modulate the arousal in the SHS (McNaughton & Gray, 2000). This is supported by studies linking BIS to amygdala-hippocampus connectivity during monetary loss (Hahn et al., 2010; Hahn et al., 2013). The hypothalamus and PAG are the main structures proposed for FFFS, however, the review did not identify any studies showing this relationship with either activity or structure of these systems. There were some findings associating BIS/FFFS traits with activity in the nearby thalamus when viewing erotic, disgusting and fear evoking (Reuter et al., 2004). The authors argued that this discrepancy may be due to difficultly directly applying a theory built of the back of animal literature to human subjects with far more complicated brain structures. On the other hand, the lack of findings may also simply be due to limitations in the literature in terms of sole psychometric assessment of the original systems that conflate BIS and FFFS, highlighting the urgent need to examine BIS and FFFS related functional and structural underpinnings using revised RST scales.

4.3: Potential additional structures for RST systems

This review has identified some common findings of relationships between RST scales and structures outside the initially proposed circuitry. BAS was associated with hippocampal functioning during priming tasks and when viewing erotic pictures (Mortensen et al., 2015; Reuter et al., 2004). The hippocampus is not included in the proposed RST circuitry for the BAS (Gray & McNaughton, 2000); however, it has been implicated in reward memory in the general

reward literature (Davidow, Foerde, Galván & Shohamy, 2016 ; Lansik, Goltstein, Lankelma, McNaughton & Pennartz, 2009). It has been argued that reward prediction is modulated by dopamine firing at cortical-striatal synapses, with greater firing for unpredicted rewards and a reduction in firing when reward is omitted (Pickering & Corr, 2008). If the BAS is responsible for reward prediction, then it must first have access to previous data. The hippocampus is widely known for its role in memory (Eichenbaum, 2017; Bird, 2017), so its role in the BAS as the hub for reward memories seems likely. The hippocampus is part of the proposed BIS circuitry, so it may be that the BAS accesses and updates its reward memories from within the BIS structure, with the BIS facilitating BAS related reward processing under certain prediction conditions.

Some studies found a relationship between BAS traits and increased activity in the insula when viewing erotic images (Customero et al., 2013b; Rueter et al., 2004) and disgusting images (Rueter et al., 2004) but reduced activity during Go/NoGo tasks (Funetas-Claramonte et al., 2016). BAS was also related to reduced GMV (Adrian-Ventura et al., 2019b). The insula has been implicated in reward prediction (Furl & Averbeck, 2011; Sescusse, Caldú, Segura & Dreher, 2013) and is connected through dopaminergic neurons to the VS indicating a potential role within the BAS (Sescusse, Caldú, Segura & Dreher, 2013). Insula activity increases during sexual arousal (Kühn & Gallinat, 2011), and BAS is related to greater sexual arousal responses (Customero et al., 2013b). However, the insula is widely regarded as a hub for risk management and processing negative stimuli (Knutson & Bossaerts, 2007; Wright, He, Shapira, Goodman & Liu, 2004). The relationship between BAS and insula activity to disgusting images is surprising due to the appetitive nature of the BAS and should be examined further (Reuter et al., 2004). However, the idea that the BAS and approach motivation is associated with only positive affect has been challenged by research indicating its role in anger (Harmon-Jones, 2003).

BAS traits were associated with reduced activity in the ACC (Van Rijn et al., 2016; Funetas-Claramonte et al., 2016; Gray & Braver, 2002; Gray et al., 2005) and with increased connectivity between the ACC and vmPFC (Adrian-Ventura et al., 2019a). The research suggests that the relationship between BAS and ACC represents cognitive control and efficiency, rather than emotion processing (Gray & Braver, 2002; Gray et al., 2005), so its potential addition to the BAS circuitry may not be justified.

4.4: Sex differences

Although most cohorts included both males and females, few controlled for sex differences or directly investigated them. Two structural studies investigated sex as a variable in their analysis, one study found differences in the GMV of the amygdala was related to BIS measures and the GMV of the NAcc was related to BAS measures, but only in males, with no relationship found for females (Adrian-Ventura et al., 2019b). Another study found a negative association between BIS and GMV in the parahippocampus and positive association between BAS and GMV in the vmPFC and inferior parietal lobe for females, but the exact opposite pattern was found in males (Li et al., 2014). Finally, one study examined gender differences in a MID task and different patterns of activity for men and women related to both SP and SR (Dingra et al., 2021). These studies highlight how the relationship between RST traits and brain structure and function may differ between the sexes. Indeed, this is supported by general trends in brain structure and functioning that indicate sex differences. Males tend to have greater overall brain volume with a higher percentage of white matter, but a lower percentage of gray matter, whilst females have a greater cerebral blood flow than males. Moreover, sex-specific differences in dopaminergic, serotonergic, and GABAergic functioning indicate that male and female brains are neurochemically distinct (Cosgrove, Mazure & Stanley, 2007). This is further supported by

psychometric studies finding sex differences in RST traits (Corr & Cooper, 2016; Heym, Ferguson & Lawrence, 2008; Tull, Gratz, Latzman, Kimbreal & Lejuez, 2010), although these differences were often not big enough to justify splitting the data by sex. Due to differences in neuroimaging and psychometric data between males and females, future studies should always include sex as part of their analysis to ascertain exactly how RST functioning differs between sexes.

4.5: Limitations of psychometric evaluation

The psychometrics used by the studies in this review leads to several limitations that need to be addressed by future work. Firstly, all the studies included in this review were flawed in their ability to examine the current conceptualization of RST due to the sole use of scales assessing original RST. The only scales that were identified by this review were the BIS/BAS scale and SRSPQ. Both scales were designed in the light of original RST theory, which did not separate the BIS and FFFS. These systems were revised and delineated over 20 years ago, based on a wealth of research that identified anxiety and fear as separate constructs (Gray & McNaughton, 2000). One study did attempt to address this by using a neuroticism scale to index BIS and the SP scale to index FFFS (Mortensen et al., 2015). However, neuroticism cannot be considered a direct measure of BIS given its 30-45-degree rotation away from BIS (Pickering, Corr & Gray, 1999). Similarly, although some argue SP is more representative of FFFS (Mortensen et al., 2015), it is generally viewed as a conflation of both systems (Corr, 2016). Finally, there are more psychometrically robust methods to assess BIS and FFFS as separate constructs that have been specifically developed to delineate these in line with the revised theory, such as the RST-PQ (Corr & Cooper, 2016), the RSQ (Smederevac, Mitrović, Čolović & Nikolašević, 2014) and the rRST-Q (Reuter, Cooper, Smillie, Markett & Montag, 2015). It is crucial that future

neuroimaging studies include a measure of revised RST to allow an examination of the BIS and FFFS as separate systems. The continued conflation of these two systems, due to an overreliance on the well-established original RST scales, severely limits our understanding and the scientific progression of RST.

Secondly, many studies opted to only use one subscale depending on the task (e.g., BAS scale for reward paradigms, BIS/FFFS for punishment paradigms). Although it may seem appropriate as the BAS is activated by appetitive stimuli and the FFFS by aversive stimuli, it does not allow for examination of the mediating role of the BIS. The BIS is responsible for mediating all goal conflicts, whether that be a classic approach/avoidance conflict or more complex conflicts such as conflicts between multiple rewards or punishments. Many of the tasks expected to only activate one system, would inherently activate the BIS as well. For example, the MID task is often used in either a solely gain or solely loss context but will often have differing levels of gain or loss. A MID task looking at small, large or no gains may not activate the FFFS, but would activate the BAS and BIS due to reward-reward conflicts. The use of single subscales is also holding back the theoretical advancement of RST. Original RST proposed that each of the subsystems were separable, in other words the sensitivities in each system are uncorrelated with the other systems. However, according to a joint subsystems hypothesis (JSH; Corr, 2002; Smillie, Pickering & Jackson, 2006), the systems are inter-dependent, with the output of the BAS and BIS being moderated by the sensitivities of the other systems, though, the FFFS output is only affected by the FFFS sensitivity (Smillie, Pickering & Jackson, 2006). Future studies should strive to test these assumptions by including all subscales in their analysis. However, it should also be noted that psychometric measures of RST may measure the functional outputs of each

system rather than their sensitivities (Pickering, 2008). As the JHS proposes that it is the sensitivities of each system that modulates the output of the other systems, currently developed scales may not be adequate for examining the JHS (Smillie, Pickering & Jackson, 2006).

A final issue with the psychometric measures used by some studies in this review comes in the form of classifying individuals as high and low on the trait measures. Possibly due to the slow uptake of revised scales of RST, and the number of competing revised RST scales, there is no standardized scoring or cut-off for classifying individuals as high or low in each trait. For example, Bunford et al., (2017) used a median split on BIS scores to form high and low BIS groups. However, by using a median split, participants can be classed as either high or low based on a difference of 1 score. Establishing normative scores and considering systems for cut-offs (e.g., 2 SDs above or below the mean or simple slope analysis) would provide more certainty on whether an individual falls into a high or low reinforcement sensitive group. This issue is exemplified by Radke et al., (2106), where using a median split resulted in a high BAS group with a mean score of 35.9 and a low BAS group with mean score of 31.1 - both of these group means fall in the highest 33% of possible scale scores and labelling latter as low BAS is questionable to say the least. It is advised that continuous psychometric data is not artificially split unless there is strong justification to do so, such as comparing extreme groups that may be of greater interest, and even this must be done cautiously (DeCoster, Gallucci & Iselin, 2011).

4.6: Limitations of task selection

The tasks used to examine RST in this review suffer from paradoxically being too simple while simultaneously being too complex. There are 3 main goals that tasks assessing RST should be able to achieve. Firstly, they should be able to attempt to activate each system individually without interference from the other systems so that each individual system can be examined.

Secondly, they should be able to activate all systems simultaneously to examine how the systems interact with each other. Finally, they need to have enough depth that they simulate the whole spectrum of defensive distance, not just the most distal levels.

A task that can activate each system separately must avoid any conflict that may activate the BIS (McNaughton & Corr, 2004). As previously mentioned, some studies looked at MID tasks as only activating one system, such as gain MID tasks only activating BAS. However, using rewards that vary in size the BIS would be active to mediate approach-approach conflicts. To activate each system separately tasks would require various levels. To individually activate the BAS the task would need to offer a reward schedule where, regardless of strategy, the participant would gain a consistent reward with no chance of losing this reward. To activate the FFFS, the task would need to have a single consistent threat where there is no chance of reward or conflict between avoiding multiple threats. There may be more difficulty in solely activating the BIS, due to its role as a mediation system. Conceptually, the BIS may only be activated when a conflict arises. This means activation of the BIS entails activation of either the BAS or FFFS first. However, this could potentially be overcome by creating a task where the outcome of the participants actions remains ambiguous until the end of the task. This ambiguity may allow for BIS activation while keeping BAS and FFFS involvement minimal. Theoretically the BIS inhibits all behaviours until it resolves goal conflict and lets one system gain dominance to achieve the optimum outcome. In a fully ambiguous task, there would be no clear optimal strategy so only the BIS should be activated trying to solve this impossible problem. Most tasks in this review are successful in generating some form of conflict, such as conflicts arising in the MID tasks mentioned earlier; however, none of the tasks used exhaustively examine or manipulate all the possible conflicts. To provide a deeper examination of RST in terms of human

behaviour and neurobiology these tasks should strive to manipulate different intensities of conflicts including both within and between system conflicts.

Finally, tasks need to have the ability to activate every level of the neural structures included in the RST systems. Brain activity in the FFFS and BIS is structured in a hierarchical fashion based on defensive distance (Gray & McNaughton, 2000). Using monetary loss to trigger FFFS and BIS activity are likely to show activity only in the higher regions of the hierarchy as they are not sufficiently aversive. To stimulate deeper regions may require some form of pain stimuli (Roy et al.,2014). Using punishments such as aversive sound blasts or electric shocks would trigger deeper activity in the amygdala and PAG. Indeed, fMRI can be compatible with tactile stimulation such as air puffs that could be used as a negative event (e.g., Kumari et al., 2007)

4.7: Limitations of this review

This review provides an overview of associations between RST scales and (f)MRI correlates, broken down by different tasks. It has made recommendations on the use of psychometric scales and task selection to help guide future research to appropriate methods for assessing neural correlates of RST in light of its revisions. What this review has not focused on are the inter-study variations in (f)MRI methodology. The studies identified varied on a number of levels such as image acquisition, image pre-processing, data analysis and the scanner used, which may impact findings and interpretations drawn. Future work could address these issues by performing an in-depth analysis to take these aspects into account, which may add to the current picture and further our understanding of RST brain correlates.

4.8: Conclusion

In conclusion, the original RST measures of BIS and BAS seem to map onto some of the proposed circuitry. There was strong support for the role of the PFC and VS in the BAS circuitry, but less evidence regarding the VPal and VTA. It was not possible to examine the BIS and FFFS separately as all the studies in this review used an original RST scale. Nevertheless, there is evidence for some of the structures related to larger defensive distances such as the PFC and cingulate cortices, but no evidence for deeper structures activated at the most proximal distances (e.g., PAG). Future studies need to adopt the use of revised RST scales, diversify the tasks used so they can target the whole spectrum of defensive distance and simplify tasks to isolate each system so their neural underpinnings can be more precisely delineated.

References

Adrián-Ventura, J., Costumero, V., Parcet, M. A., & Ávila, C. (2019). Linking personality and brain anatomy: a structural MRI approach to Reinforcement Sensitivity Theory. *Social cognitive and affective neuroscience*, *14*(3), 329-338.

Adrián-Ventura, J., Costumero, V., Parcet, M. A., & Ávila, C. (2019). Reward network connectivity "at rest" is associated with reward sensitivity in healthy adults: a resting-state fMRI study. *Cognitive, Affective, & Behavioral Neuroscience*, *19*(3), 726-736.

Angelides, N. H., Gupta, J., & Vickery, T. J. (2017). Associating resting-state connectivity with trait impulsivity. *Social cognitive and affective neuroscience*, *12*(6), 1001-1008.

Apergis-Schoute, A. M., Bijleveld, B., Gillan, C. M., Fineberg, N. A., Sahakian, B. J., & Robbins, T. W. (2018). Hyperconnectivity of the ventromedial prefrontal cortex in obsessive-compulsive disorder. *Brain and neuroscience advances*, *2*, 2398212818808710.

Arias-Carrión, O., Stamelou, M., Murillo-Rodríguez, E., Menéndez-González, M., & Pöppel, E. (2010). Dopaminergic reward system: a short integrative review. *International archives of medicine*, *3*(1), 1-6.

Assareh, N., Sarrami, M., Carrive, P., & McNally, G. P. (2016). The organization of defensive behavior elicited by optogenetic excitation of rat lateral or ventrolateral periaqueductal gray. *Behavioral neuroscience*, *130*(4), 406.

Avila, C., Garbin, G., Sanjuán, A., Forn, C., Barrós-Loscertales, A., Bustamante, J. C., ... & Parcet, M. A. (2012). Frontostriatal response to set switching is moderated by reward sensitivity. *Social cognitive and affective neuroscience*, *7*(4), 423-430.

Balleine, B. W., Delgado, M. R., & Hikosaka, O. (2007). The role of the dorsal striatum in reward and decision-making. *Journal of Neuroscience*,*27*(31), 8161-8165.

Balconi, M., Angioletti, L., De Filippis, D., & Bossola, M. (2019). Association between fatigue, motivational measures (BIS/BAS) and semi-structured psychosocial interview in hemodialytic treatment. *BMC psychology*, *7*(1), 49.

Barrós-Loscertales, A., Meseguer, V., Sanjuán, A., Belloch, V., Parcet, M. A., Torrubia, R., & Ávila, C. (2006). Behavioral inhibition system activity is associated with increased amygdala and hippocampal gray matter volume: a voxel-based morphometry study. *Neuroimage*, *33*(3), 1011-1015.

Barrós- Loscertales, A., Meseguer, V., Sanjuán, A., Belloch, V., Parcet, M. A., Torrubia, R., & Avila, C. (2006). Striatum gray matter reduction in males with an overactive behavioral activation system. *European Journal of Neuroscience*, *24*(7), 2071-2074.

Barrós-Loscertales, A., Ventura-Campos, N., Sanjuán-Tomás, A., Belloch, V., Parcet, M. A., & Ávila, C. (2010). Behavioral activation system modulation on brain activation during appetitive and aversive stimulus processing. *Social Cognitive and Affective Neuroscience*, *5*(1), 18-28.

Baxter, M. G., & Murray, E. A. (2002). The amygdala and reward. *Nature reviews neuroscience*, *3*(7), 563-573.

Beaver, J. D., Lawrence, A. D., Van Ditzhuijzen, J., Davis, M. H., Woods, A., & Calder, A. J. (2006). Individual differences in reward drive predict neural responses to images of food. *Journal of Neuroscience*, *26*(19), 5160-5166.

Bird, C. M. (2017). The role of the hippocampus in recognition memory. *Cortex*, *93*, 155-165.

Blanchard, R.J. and Blanchard, D.C. (1990a) 'An ethoexperimental analysis of defense, fear and anxiety', in N. McNaughton and G. Andrews (eds), *Anxiety*. Dunedin: Otago University Press, pp. 12–133.

Blanchard, D. C., & Blanchard, R. J (1990b). Anti-predator defence as models of animal fear and anxiety. In P. F. Brain, S. Parmigiani, R. J. Blanchard, & D. Blanchard (Eds.), *Fear and defence* (pp. 89-105). Chur, Switzerland: Harwood Academic.

Blanchard, R. J., Griebel, G., Henrie, J. A., & Blanchard, D. C. (1997). Differentiation of anxiolytic and panicolytic drugs by effects on rat and mouse defense test batteries. *Neuroscience & Biobehavioral Reviews*, *21*(6), 783-789.

Blanchard, D. C., Griebel, G., & Blanchard, R. J. (2001). Mouse defensive behaviors: pharmacological and behavioral assays for anxiety and panic. *Neuroscience & Biobehavioral Reviews*, *25*(3), 205-218.

Bossola, M., Angioletti, L., Di Stasio, E., Vulpio, C., De Filippis, D., & Balconi, M. (2020). Reward (BIS/BAS) mechanisms and fatigue in patients on chronic hemodialysis. *Psychology, health & medicine*, *25*(6), 710-718.

Botvinick, M. M., Cohen, J. D., & Carter, C. S. (2004). Conflict monitoring and anterior cingulate cortex: an update. *Trends in cognitive sciences*, *8*(12), 539-546.

Breiter, H. C., Aharon, I., Kahneman, D., Dale, A., & Shizgal, P. (2001). Functional imaging of neural responses to expectancy and experience of monetary gains and losses. *Neuron*, *30*(2), 619-639.

Bunford, N., Roberts, J., Kennedy, A. E., & Klumpp, H. (2017). Neurofunctional correlates of behavioral inhibition system sensitivity during attentional control are modulated by perceptual load. *Biological Psychology*, *127*, 10-17.

Carver, C. S., & White, T. L. (1994). Behavioral inhibition, behavioral activation, and affective responses to impending reward and punishment: the BIS/BAS scales. *Journal of personality and social psychology*, *67*(2), 319.

Cherbuin, N., Windsor, T. D., Anstey, K. J., Maller, J. J., Meslin, C., & Sachdev, P. S. (2008). Hippocampal volume is positively associated with behavioural inhibition (BIS) in a large community-based sample of mid-life adults: the PATH through life study. *Social cognitive and affective neuroscience*, *3*(3), 262-269.

Corr, P. J. (2002). JA Gray's reinforcement sensitivity theory: Tests of the joint subsystems hypothesis of anxiety and impulsivity. *Personality and individual differences*, *33*(4), 511-532.

Corr, P. J. (2016). Reinforcement sensitivity theory of personality questionnaires: Structural survey with recommendations. *Personality and Individual Differences*, 89, 60-64.

Corr, P. J., & Cooper, A. J. (2016). The Reinforcement Sensitivity Theory of Personality Questionnaire (RST-PQ): Development and validation. *Psychological assessment*, *28*(11), 1427.

Costumero, V., Barrós-Loscertales, A., Bustamante, J. C., Ventura-Campos, N., Fuentes, P., Rosell-Negre, P., & Ávila, C. (2013b). Reward sensitivity is associated with brain activity during erotic stimulus processing. *PLoS One*, *8*(6), e66940.

Costumero, V., Barrós- Loscertales, A., Bustamante, J. C., Ventura- Campos, N., Fuentes, P., & Ávila, C. (2013a). Reward sensitivity modulates connectivity among reward brain areas during processing of anticipatory reward cues. *European Journal of Neuroscience*, *38*(3), 2399-2407.

Costumero, V., Barrós-Loscertales, A., Fuentes, P., Rosell-Negre, P., Bustamante, J. C., & Ávila, C. (2016). BAS-drive trait modulates dorsomedial striatum activity during reward response-outcome associations. *Brain imaging and behavior*, *10*(3), 869-879.

Costumero, V., Barrós-Loscertales, A., Bustamante, J. C., Fuentes, P., Rosell-Negre, P., Ventura-Campos, N., & Avila, C. (2015). A new window to understanding individual differences in reward sensitivity from attentional networks. *Brain Structure and Function*, *220*(3), 1807-1821.

Davidow, J. Y., Foerde, K., Galván, A., & Shohamy, D. (2016). An upside to reward sensitivity: the hippocampus supports enhanced reinforcement learning in adolescence. *Neuron*, *92*(1), 93-99.

Davis, M. (1992). The role of the amygdala in fear and anxiety. *Annual review of neuroscience*, *15*(1), 353-375.

Davis, M., Walker, D. L., Miles, L., & Grillon, C. (2010). Phasic vs sustained fear in rats and humans: role of the extended amygdala in fear vs anxiety. *Neuropsychopharmacology*, *35*(1), 105-135.

Deng, H., Xiao, X., & Wang, Z. (2016). Periaqueductal gray neuronal activities underlie different aspects of defensive behaviors. *Journal of Neuroscience*, *36*(29), 7580-7588.

Dong, G., Li, H., Wang, Y., & Potenza, M. N. (2018). Individual differences in self-reported reward-approach tendencies relate to resting-state and reward-task-based fMRI measures. *International Journal of Psychophysiology*, *128*, 31-39.

Downes, M. J., Brennan, M. L., Williams, H. C., & Dean, R. S. (2016). Development of a critical appraisal tool to assess the quality of cross-sectional studies (AXIS). *BMJ open*, *6*(12), e011458.

Eichenbaum, H. (2017). The role of the hippocampus in navigation is memory. *Journal of neurophysiology*, *117*(4), 1785-1796.

Einarsson, E. Ö., & Nader, K. (2012). Involvement of the anterior cingulate cortex in formation, consolidation, and reconsolidation of recent and remote contextual fear memory. *Learning & memory*, *19*(10), 449-452.

Eryilmaz, H., Rodriguez-Thompson, A., Tanner, A. S., Giegold, M., Huntington, F. C., & Roffman, J. L. (2017). Neural determinants of human goal-directed vs. habitual action control and their relation to trait motivation. *Scientific reports*, *7*(1), 1-11.

Fiddick, L. (2011). There is more than the amygdala: potential threat assessment in the cingulate cortex. *Neuroscience & Biobehavioral Reviews*, *35*(4), 1007-1018.

Fineberg, N. A., Apergis-Schoute, A. M., Vaghi, M. M., Banca, P., Gillan, C. M., Voon, V., ... & Bullmore, E. T. (2018). Mapping compulsivity in the DSM-5 obsessive compulsive and related disorders: cognitive domains, neural circuitry, and treatment. *International Journal of Neuropsychopharmacology*, *21*(1), 42-58.

Firth, J., Standen, B.,Sumich, A & Heym, N (2022) The neural correlates of Reinforcement Sensitivity Theory: A systematic review of the EEG literature [Unpublished Manuscript]. NTU Psychology, Nottingham Trent University.

Fox, A. S., & Shackman, A. J. (2019). The central extended amygdala in fear and anxiety: Closing the gap between mechanistic and neuroimaging research. *Neuroscience letters*, *693*, 58-67.

Fuentes-Claramonte, P., Ávila, C., Rodríguez-Pujadas, A., Costumero, V., Ventura-Campos, N., Bustamante, J. C., ... & Barrós-Loscertales, A. (2016). Characterizing individual differences in reward sensitivity from the brain networks involved in response inhibition. *Neuroimage*, *124*, 287-299.

Fuentes-Claramonte, P., Ávila, C., Rodríguez-Pujadas, A., Costumero, V., Ventura-Campos, N., Bustamante, J. C., ... & Barrós-Loscertales, A. (2016). Inferior frontal cortex activity is

modulated by reward sensitivity and performance variability. *Biological Psychology*, *114*, 127-137.

Fuentes-Claramonte, P., Ávila, C., Rodríguez-Pujadas, A., Ventura-Campos, N., Bustamante, J. C., Costumero, V., ... & Barrós-Loscertales, A. (2015). Reward sensitivity modulates brain activity in the prefrontal cortex, ACC and striatum during task switching. *PLoS One*, *10*(4), e0123073.

Furl, N., & Averbeck, B. B. (2011). Parietal cortex and insula relate to evidence seeking relevant to reward-related decisions. *Journal of Neuroscience*, *31*(48), 17572-17582.

Frankland, P. W., Bontempi, B., Talton, L. E., Kaczmarek, L., & Silva, A. J. (2004). The involvement of the anterior cingulate cortex in remote contextual fear memory. *Science*, *304*(5672), 881-883.

Gray, J. A. (1982). Précis of The neuropsychology of anxiety: An enquiry into the functions of the septo-hippocampal system. *Behavioral and Brain Sciences, 5*(3), 469-484.

Gray, J. R., & Braver, T. S. (2002). Personality predicts working-memory—related activation in the caudal anterior cingulate cortex. *Cognitive, Affective, & Behavioral Neuroscience, 2(1),* 64-75.

Gray, J. R., Burgess, G. C., Schaefer, A., Yarkoni, T., Larsen, R. J., & Braver, T. S. (2005). Affective personality differences in neural processing efficiency confirmed using fMRI. *Cognitive, Affective, & Behavioral Neuroscience*, *5*(2), 182-190.

Glover, G. H. (2011). Overview of functional magnetic resonance imaging. Neurosurgery Clinics, 22(2), 133-139.

Griebel, G., Blanchard, D. C., Jung, A., Masuda, C. K., & Blanchard, R. J. (1995). 5-HT1A agonists modulate mouse antipredator defensive behavior differently from the 5-HT2A antagonist pirenperone. *Pharmacology Biochemistry and Behavior*, *51*(2-3), 235-244.

Gross, C. T., & Canteras, N. S. (2012). The many paths to fear. *Nature Reviews Neuroscience*, *13*(9), 651-658.

Gui, X. U. E., Chuansheng, C. H. E. N., Zhong-Lin, L. U., & Qi, D. O. N. G. (2010). Brain imaging techniques and their applications in decision-making research. Xin li xue bao. Acta psychologica Sinica, 42(1), 120.

Haber, S. N. (2011). Neuroanatomy of Reward: A View from the Ventral Striatum. *Neurobiology of sensation and reward*, 235.

Haber, S. N., & Knutson, B. (2010). The reward circuit: linking primate anatomy and human imaging. *Neuropsychopharmacology*, *35*(1), 4-26.

Hahn, T., Dresler, T., Ehlis, A. C., Pyka, M., Dieler, A. C., Saathoff, C., ... & Fallgatter, A. J. (2012). Randomness of resting-state brain oscillations encodes Gray's personality trait. *Neuroimage*, *59*(2), 1842-1845.

Hahn, T., Dresler, T., Ehlis, A. C., Plichta, M. M., Heinzel, S., Polak, T., ... & Fallgatter, A. J. (2009). Neural response to reward anticipation is modulated by Gray's impulsivity. *Neuroimage*, *46*(4), 1148-1153.

Hahn, T., Dresler, T., Plichta, M. M., Ehlis, A. C., Ernst, L. H., Markulin, F., ... & Fallgatter, A. J. (2010). Functional amygdala-hippocampus connectivity during anticipation of aversive

events is associated with Gray's trait "sensitivity to punishment". *Biological psychiatry*, *68*(5), 459-464.

Hahn, T., Dresler, T., Pyka, M., Notebaert, K., & Fallgatter, A. J. (2013). Local synchronization of resting-state dynamics encodes gray's trait anxiety. *PLoS One*, *8*(3), e58336.

Hahn, T., Heinzel, S., Dresler, T., Plichta, M. M., Renner, T. J., Markulin, F., ... & Fallgatter, A. J. (2011). Association between reward- related activation in the ventral striatum and trait reward sensitivity is moderated by dopamine transporter genotype. *Human brain mapping*, *32*(10), 1557-1565.

Hahn, T., Heinzel, S., Notebaert, K., Dresler, T., Reif, A., Lesch, K. P., ... & Fallgatter, A. J. (2013). The tricks of the trait: neural implementation of personality varies with genotype-dependent serotonin levels. *Neuroimage*, *81*, 393-399.

Harmon-Jones, E. (2003). Anger and the behavioral approach system. *Personality and Individual differences*, 35(5), 995-1005.

Heimer, L., De Olmos, J. S., Alheid, G. F., Pearson, J., Sakamoto, N., Shinoda, K., ... & Switzer, R. C. (1999). The human basal forebrain. Part II. *Handbook of chemical neuroanatomy*, 15, 57-226.

Heym, N., Ferguson, E., & Lawrence, C. (2008). An evaluation of the relationship between Gray's revised RST and Eysenck's PEN: Distinguishing BIS and FFFS in Carver and White's BIS/BAS scales. *Personality and Individual Differences*, *45*(8), 709-715.

Jackson, C. J. (2009). Jackson-5 scales of revised Reinforcement Sensitivity Theory (r-RST) and their application to dysfunctional real world outcomes. *Journal of Research in Personality*, *43*(4), 556-569.

Jeena, R. S., & Kumar, S. (2013). A comparative analysis of MRI and CT brain images for stroke diagnosis. In 2013 Annual International Conference on Emerging Research Areas and 2013 International Conference on Microelectronics, Communications and Renewable Energy (pp. 1-5). IEEE.

Keifer Jr, O. P., Hurt, R. C., Ressler, K. J., & Marvar, P. J. (2015). The physiology of fear: reconceptualizing the role of the central amygdala in fear learning. *Physiology*, *30*(5), 389-401.

Knutson, B., Adams, C. M., Fong, G. W., & Hommer, D. (2001). Anticipation of increasing monetary reward selectively recruits nucleus accumbens. *Journal of Neuroscience*, *21*(16), RC159-RC159.

Knutson, B., & Bossaerts, P. (2007). Neural antecedents of financial decisions. *Journal of Neuroscience*, *27*(31), 8174-8177.

Kühn, S., & Gallinat, J. (2011). A quantitative meta- analysis on cue- induced male sexual arousal. *The journal of sexual medicine*, *8*(8), 2269-2275.

Kumari, V., Antonova, E., Geyer, M. A., Ffytche, D., Williams, S. C., & Sharma, T. (2007). A fMRI investigation of startle gating deficits in schizophrenia patients treated with typical or atypical antipsychotics. *International Journal of Neuropsychopharmacology*, *10*(4), 463-477.

Krupić, D., & Corr, P. J. (2017). Moving forward with the BAS: Towards a neurobiology of multidimensional model of approach motivation. *Psychological Topics, 26*(1), 25-45.

Krupić, D., Corr, P. J., Ručević, S., Križanić, V., & Gračanin, A. (2016). Five reinforcement sensitivity theory (RST) of personality questionnaires: Comparison, validity and generalization. *Personality and Individual Differences, 97*, 19-24.

Lansink, C. S., Goltstein, P. M., Lankelma, J. V., McNaughton, B. L., & Pennartz, C. M. (2009). Hippocampus leads ventral striatum in replay of place-reward information. *PLoS Biol, 7*(8), e1000173.

LeDoux, J. E. (1994). Emotion, memory and the brain. *Scientific American, 270*(6), 50-57.

Leech, R., & Sharp, D. J. (2014). The role of the posterior cingulate cortex in cognition and disease. *Brain, 137*(1), 12-32.

Levita, L., Bois, C., Healey, A., Smyllie, E., Papakonstantinou, E., Hartley, T., & Lever, C. (2014). The Behavioural Inhibition System, anxiety and hippocampal volume in a non-clinical population. *Biology of mood & anxiety disorders, 4*(1), 1-10.

Li, Y., Qiao, L., Sun, J., Wei, D., Li, W., Qiu, J., ... & Shi, H. (2014). Gender-specific neuroanatomical basis of behavioral inhibition/approach systems (BIS/BAS) in a large sample of young adults: a voxel-based morphometric investigation. *Behavioural brain research, 274*, 400-408.

Liu, X., Hairston, J., Schrier, M., & Fan, J. (2011). Common and distinct networks underlying reward valence and processing stages: a meta-analysis of functional neuroimaging studies. *Neuroscience & Biobehavioral Reviews, 35*(5), 1219-1236.

Luking, K. R., & Barch, D. M. (2013). Candy and the brain: neural response to candy gains and losses. *Cognitive, Affective, & Behavioral Neuroscience*, *13*(3), 437-451.

McNaughton, N. (1997). Cognitive dysfunction resulting from hippocampal hyperactivity—a possible cause of anxiety disorder?. *Pharmacology Biochemistry and Behavior*, *56*(4), 603-611.

McNaughton, N., & Gray, J. A. (2000). Anxiolytic action on the behavioural inhibition system implies multiple types of arousal contribute to anxiety. *Journal of affective disorders*, *61*(3), 161-176.

Milad, M. R., Quirk, G. J., Pitman, R. K., Orr, S. P., Fischl, B., & Rauch, S. L. (2007). A role for the human dorsal anterior cingulate cortex in fear expression. *Biological psychiatry*, *62*(10), 1191-1194.

Milne, E., & Grafman, J. (2001). Ventromedial prefrontal cortex lesions in humans eliminate implicit gender stereotyping. *Journal of Neuroscience*, *21*(12), RC150-RC150.

Moher, D., Liberati, A., Tetzlaff, J., Altman, D. G., & Prisma Group. (2009). Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. *PLoS medicine*, *6(7)*, e1000097.

Mortensen, J. A., Lehn, H., Evensmoen, H. R., & Håberg, A. K. (2015). Evidence for an antagonistic interaction between reward and punishment sensitivity on striatal activity: A verification of the Joint Subsystems Hypothesis. *Personality and Individual Differences*, *74*, 214-219.

Motta, S. C., Carobrez, A. P., & Canteras, N. S. (2017). The periaqueductal gray and primal emotional processing critical to influence complex defensive responses, fear learning and reward seeking. *Neuroscience & Biobehavioral Reviews*, *76*, 39-47.

Motta, S. C., Goto, M., Gouveia, F. V., Baldo, M. V., Canteras, N. S., & Swanson, L. W. (2009). Dissecting the brain's fear system reveals the hypothalamus is critical for responding in subordinate conspecific intruders. *Proceedings of the National Academy of Sciences*, *106*(12), 4870-4875.

Murray, E. A. (2007). The amygdala, reward and emotion. *Trends in cognitive sciences*, *11*(11), 489-497.

Neseliler, S., Tannenbaum, B., Zacchia, M., Larcher, K., Coulter, K., Lamarche, M., ... & Dagher, A. (2017). Academic stress and personality interact to increase the neural response to high-calorie food cues. *Appetite*, *116*, 306-314.

O'Doherty, J., Kringelbach, M. L., Rolls, E. T., Hornak, J., & Andrews, C. (2001). Abstract reward and punishment representations in the human orbitofrontal cortex. *Nature neuroscience*, *4*(1), 95-102.

O'Doherty, J. P., Buchanan, T. W., Seymour, B., & Dolan, R. J. (2006). Predictive neural coding of reward preference involves dissociable responses in human ventral midbrain and ventral striatum. *Neuron*, *49*(1), 157-166.

Ogawa, S., Lee, T. M., Stepnoski, R., Chen, W., Zhu, X. H., & Ugurbil, K. (2000). An approach to probe some neural systems interaction by functional MRI at neural time scale down to milliseconds. *Proceedings of the National Academy of Sciences, 97(20)*, 11026-11031.

Oldham, S., Murawski, C., Fornito, A., Youssef, G., Yücel, M., & Lorenzetti, V. (2018). The anticipation and outcome phases of reward and loss processing: A neuroimaging meta-analysis of the monetary incentive delay task. *Human brain mapping*, *39*(8), 3398-3418.

Pascucci, D., Hickey, C., Jovicich, J., & Turatto, M. (2017). Independent circuits in basal ganglia and cortex for the processing of reward and precision feedback. *Neuroimage*, *162*, 56-64.

Peters, J., & Büchel, C. (2010). Neural representations of subjective reward value. *Behavioural brain research*, *213*(2), 135-141.

Pickering, A. D. (2008). Formal and computational models of Reinforcement Sensitivity Theory. *The reinforcement sensitivity theory of personality*, 453.

Pickering, A. D., & Corr, P. J. (2008). JA Gray's reinforcement sensitivity theory (RST) of personality. *The SAGE handbook of personality: Theory and assessment personality measurement and testing*, *2*, 239-255.

Pickering, A. D., Corr, P. J., & Gray, J. A. (1999). Interactions and reinforcement sensitivity theory: A theoretical analysis of Rusting and Larsen (1997).

Pickering, A. D., & Smillie, L. D. (2008). The behavioural activation system: Challenges and opportunities. *The reinforcement sensitivity theory of personality*, 120-154.

Qiu, C., Liao, W., Ding, J., Feng, Y., Zhu, C., Nie, X., ... & Gong, Q. (2011). Regional homogeneity changes in social anxiety disorder: a resting-state fMRI study. *Psychiatry Research: Neuroimaging*, *194*(1), 47-53.

Quadflieg, S., Turk, D. J., Waiter, G. D., Mitchell, J. P., Jenkins, A. C., & Macrae, C. N. (2009). Exploring the neural correlates of social stereotyping. *Journal of Cognitive Neuroscience*, *21*(8), 1560-1570.

Radke, S., Seidel, E. M., Eickhoff, S. B., Gur, R. C., Schneider, F., Habel, U., & Derntl, B. (2016). When opportunity meets motivation: neural engagement during social approach is linked to high approach motivation. *NeuroImage*, *127*, 267-276.

Reuter, M., Cooper, A. J., Smillie, L. D., Markett, S., & Montag, C. (2015). A new measure for the revised reinforcement sensitivity theory: Psychometric criteria and genetic validation. *Frontiers in systems neuroscience*, 9, 38.

Reuter, M., Stark, R., Hennig, J., Walter, B., Kirsch, P., Schienle, A., & Vaitl, D. (2004). Personality and emotion: test of Gray's personality theory by means of an fMRI study. *Behavioral Neuroscience*, *118*(3), 462.

Roy, M., Shohamy, D., Daw, N., Jepma, M., Wimmer, G. E., & Wager, T. D. (2014). Representation of aversive prediction errors in the human periaqueductal gray. *Nature neuroscience*, *17*(11), 1607-1612.

Rushworth, M. F., Noonan, M. P., Boorman, E. D., Walton, M. E., & Behrens, T. E. (2011). Frontal cortex and reward-guided learning and decision-making. *Neuron*, *70*(6), 1054-1069.

Sescousse, G., Caldú, X., Segura, B., & Dreher, J.-C. C. (2013). Processing of primary and secondary rewards: a quantitative meta-analysis and review of human functional neuroimaging studies. Neuroscience and Biobehavioral Reviews, 37(4), 681–696.

Simon, J. J., Walther, S., Fiebach, C. J., Friederich, H. C., Stippich, C., Weisbrod, M., & Kaiser, S. (2010). Neural reward processing is modulated by approach-and avoidance-related personality traits. *Neuroimage*, *49*(2), 1868-1874.

Smederevac, S., Mitrović, D., Čolović, P., & Nikolašević, Ž. (2014). Validation of the measure of revised reinforcement sensitivity theory constructs. *Journal of Individual Differences*.

Smillie, L. D. (2008). What is reinforcement sensitivity? Neuroscience paradigms for approach-avoidance process theories of personality. *European Journal of Personality*, 22(5), 359-384.

Smillie, L. D., Pickering, A. D., & Jackson, C. J. (2006). The new reinforcement sensitivity theory: Implications for personality measurement. *Personality and Social Psychology Review*, *10*(4), 320-335.

Smith, K. S., Tindell, A. J., Aldridge, J. W., & Berridge, K. C. (2009). Ventral pallidum roles in reward and motivation. *Behavioural brain research*, *196*(2), 155-167.

Staudinger, M. R., Erk, S., & Walter, H. (2011). Dorsolateral prefrontal cortex modulates striatal reward encoding during reappraisal of reward anticipation. *Cerebral cortex*, *21*(11), 2578-2588.

Strauman, T. J., Detloff, A. M., Sestokas, R., Smith, D. V., Goetz, E. L., Rivera, C., & Kwapil, L. (2013). What shall I be, what must I be: neural correlates of personal goal activation. *Frontiers in integrative neuroscience*, *6*, 123.

Sun, J., Luo, Y., Chang, H., Zhang, R., Liu, R., Jiang, Y., & Xi, H. (2020). The Mediating Role of Cognitive Emotion Regulation in BIS/BAS Sensitivities, Depression, and Anxiety

Among Community-Dwelling Older Adults in China. *Psychology Research and Behavior Management*, *13*, 939.

Tang, J., Ko, S., Ding, H. K., Qiu, C. S., Calejesan, A. A., & Zhuo, M. (2005). Pavlovian fear memory induced by activation in the anterior cingulate cortex. *Molecular pain*, *1*, 1744-8069.

Teyler, T. J., & DiScenna, P. (1985). The role of hippocampus in memory: a hypothesis. *Neuroscience & Biobehavioral Reviews*, *9*(3), 377-389.

Torrubia, R., Avila, C., Moltó, J., & Caseras, X. (2001). The Sensitivity to Punishment and Sensitivity to Reward Questionnaire (SPSRQ) as a measure of Gray's anxiety and impulsivity dimensions. *Personality and individual differences*, *31*(6), 837-862.

Trutti, A. C., Mulder, M. J., Hommel, B., & Forstmann, B. U. (2019). Functional neuroanatomical review of the ventral tegmental area. *NeuroImage*, *191*, 258-268.

Tull, M. T., Gratz, K. L., Latzman, R. D., Kimbrel, N. A., & Lejuez, C. W. (2010). Reinforcement sensitivity theory and emotion regulation difficulties: A multimodal investigation. *Personality and Individual Differences*, *49*(8), 989-994.

van Rijn, I., Griffioen-Roose, S., de Graaf, C., & Smeets, P. A. (2016). Neural processing of calories in brain reward areas can be modulated by reward sensitivity. *Frontiers in behavioral neuroscience*, *9*, 371.

Walker, B. R., & Jackson, C. J. (2017). Examining the validity of the revised Reinforcement Sensitivity Theory scales. *Personality and Individual Differences*, *106*, 90-94.

Wallace, L., Heym, N., Sumich, A., & Fido, D. (2020). A systematic review on the current conceptualisations of successful psychopathy. https://doi.org/10.31234/osf.io/wkjrm

Wallis, J. D., & Kennerley, S. W. (2010). Heterogeneous reward signals in prefrontal cortex. *Current opinion in neurobiology*, *20*(2), 191-198.

Wheelock, M. D., Sreenivasan, K. R., Wood, K. H., Ver Hoef, L. W., Deshpande, G., & Knight, D. C. (2014). Threat-related learning relies on distinct dorsal prefrontal cortex network connectivity. *Neuroimage*, *102*, 904-912.

Wright, P., He, G., Shapira, N. A., Goodman, W. K., & Liu, Y. (2004). Disgust and the insula: fMRI responses to pictures of mutilation and contamination. *Neuroreport*, *15*(15), 2347-2351.

Xu, J., Kober, H., Carroll, K. M., Rounsaville, B. J., Pearlson, G. D., & Potenza, M. N. (2012). White matter integrity and behavioral activation in healthy subjects. *Human brain mapping*, *33*(4), 994-1002.

Zhao, X. H., Wang, P. J., Li, C. B., Hu, Z. H., Xi, Q., Wu, W. Y., & Tang, X. W. (2007). Altered default mode network activity in patient with anxiety disorders: an fMRI study. *European journal of radiology*, *63*(3), 373-378.

Abstract

Objectives

Reinforcement Sensitivity Theory (RST) is a theory of motivation, emotion and learning, that has been translated into an account of personality. RST proposes neural structures that form the basis of systems responsible for reward (BAS), punishment (FFFS) and conflict processing (BIS). This systematic review collated studies examining psychometric measures of RST alongside structural and function MRI data to (i) examine how psychometric RST is associated with the proposed neural topologies of RST, (ii) identify any common associations between psychometric RST and other brain regions, and (iii) provide recommendations for advancing the current literature base.

Methods

Initial search terms identified 10952 papers. After processing, 39 papers that investigated the association between RST scales and neural functioning in healthy adult samples were included in this review.

Results

There was general support for associations between the BAS and the structure/activity of the pre-frontal cortex and ventral striatum with some additional findings for the ventral pallidum and ventral tegmental area. There was also some support for associations between BIS/FFFS and structure/activity of frontal regions, cingulate cortices and the amygdala.

Conclusions

Overall, psychometric correlates of RST were associated with activity in proposed neural circuitry, with the most consistent support being found for the BAS; however, psychometric and experimental limitations still hamper the differentiation of the BIS and FFFS systems in their activation of deeper brain networks. Future studies need to include revised RST scales that separate the BIS and FFFS and implement more rigorous tasks that allow for the examination of each system both independently and codependently.

Keywords: Reinforcement sensitivity theory, Magnetic resonance imaging, systematic review

Public Significance Statement

This paper examined the neural correlates of reinforcement sensitivity theory (RST) by systematically reviewing (f)MRI literature that compared findings with a psychometric measure of RST. Findings generally support the neural structures laid out by RST for the behavioral activation system and there was some support for the behavioral inhibition system and fight-flight-freeze system. Future research needs to address the issues identified by this review, mainly the reluctance to use a psychometric scale that encapsulates revisions to the theory.

1 Introduction

1.1 Reinforcement Sensitivity Theory

Reinforcement sensitivity theory (RST), first posited by Jeffery Gray in 1982, is a neurobiological account of motivation, emotion and learning, that has been subsequently translated into an account of personality (Smillie, Pickering & Jackson, 2008). Based on animal research, RST was initially concerned with examining anxiety and classifying the underlying brain systems involved. After evidence indicating that the functioning of these systems varied between individuals in a stable manner, a theory of personality based on motivation and emotion was born (Gray & McNaughton, 2000). The original theory (Gray, 1982) proposed 2 neurobiological systems: the behavioral approach system (BAS) modulating appetitive motivation and the behavioral inhibition system (BIS) modulating aversive motivation. The BAS was sensitive to conditioned reward and related to trait impulsivity. The BIS was sensitive to conditioned aversive and high intensity stimuli and associated with trait anxiety.

By the late 1990's a wealth of research emerged that indicated that fear and anxiety were distinct processes. Firstly, animal studies found that defensive behaviours could be divided and differentiated by orientation to the threat, with one division of behaviours orientated to cautiously approaching threat and the other division orientated to escaping the threat (Blanchard & Blanchard, 1990a, 1990b). This division was further supported by studies finding anxiolytics affected defensive behaviours orientated towards threat while not affecting those orientated away from threat, whereas the opposite was found for panicolytics (Blanchard, Griebel, & Blanchard, 2001; Blanchard, Griebel, Henrie & Blanchard, 1997; Griebel, Blanchard, Jung, Masuda, & Blanchard, 1995). Based on these divisions in defensive behaviours, RST was substantially revised (Gray & McNaughton, 2000).

As the BAS is not a defensive system it remained largely unchanged (although it is now responsible for processing all appetitive stimuli, not just conditioned), however, the role of the BIS changed significantly with the addition of the flight-fight-freeze system (FFFS), which is now responsible for processing all aversive stimuli (conditioned and unconditioned), behaviourally represented by defensive/active avoidance behaviours and emotionally expressed as fear (McNaughton & Corr, 2004). The BIS is now proposed to be a mediating system for approach-avoidance conflicts between BAS and FFFS activation (though also for approach-approach or avoidance-avoidance conflicts). Its output is characterized by behavioural inhibition to allow for conflict monitoring and increased risk assessment, behaviourally expressed as defensive approach/passive avoidance behaviour and emotionally reflected in anxiety responses (McNaughton & Corr, 2004). Alongside proposing the behavioural and emotional functioning of these systems, RST outlines the neural structures and pathways that physically underpin these systems. The proposed neural topology of each system will be discussed, starting with the BAS and moving on to the hierarchically organised BIS and FFFS. Psychometric measurement of RST will be discussed, followed by the aims of this review.

1.2 The Behavioral Approach System

The BAS is proposed to be located in neural structures that are responsible for processing reward - namely the dopaminergic system consisting of the ventral tegmental area (VTA), ventral palidum (VPal), ventral striatum (VS) and prefrontal cortex (PFC; Gray & McNaughton, 2000). Together, these structures form the majority of the mesocorticolimbic dopamine system, also referred to as the reward system (Arias-Carrión et al., 2010; Haber, 2011). The first component, the VTA, is one of the main dopaminergic structures in the brain, alongside the

substantia nigra (Trutti, Mulder, Hommel & Forstmann, 2019), though due to their proximity, imaging studies struggle to precisely differentiate these two structures (Trutti, Mulder, Hommel & Forstmann, 2019). The VTA has two dopaminergic pathways: The mesolimbic pathway connects the VTA to the nucleus accumbens (NAcc), which is the primary structure of the VS. The mesocortical pathway connects the VTA to frontal areas, predominantly to the dorsolateral PFC (dlPFC). These dopamine pathways fire in response to both primary and conditioned reward (Pickering & Smillie, 2008) and play a significant role in reward motivation, processing, and learning (Haber & Knutson, 2010; Pickering & Gray, 2001).

The VPal is located below the striatum and has connections within the reward system to the VTA and VS, as well as projections outside to the limbic system (see Haber & Knutson, 2010 for review). It has been found to play a role in processing a wide range of rewards, such as food, sex, and money (Smith, Tindell, Aldridge & Berridge, 2009), and is proposed to code hedonic and motivational salience, with suggestions that it may be the final pathway for reward (Smith, Tindell, Aldridge & Berridge, 2009).

The VS is mainly comprised of the NAcc but is still loosely defined in humans and may contain parts of the caudate and putamen that are generally considered as part of the dorsal striatum (see Haber & Knutson, 2010 for review). The NAcc receives inputs from a wide array of areas ranging from the PFC to the brain stem and outputs to the VTA and VPal, as well as the hypothalamus and bed nucleus of the stria terminalis (Haber & Knutson, 2010). Striatal activity increases during processing of both primary (e.g., consumption of food) and secondary (e.g., monetary gain) rewards (O'Doherty, Buchanan, Seymour & Dolan, 2006; Breiter, Aharon, Kahneman, Dale & Shizgal, 2001; Knutson, Adams, Fong & Hommer, 2001).

The final structure of the proposed BAS circuitry is the PFC, which has a range of sub areas involved in reward processing. Firstly, the dorsolateral PFC is the gateway for the mesocortical dopamine pathway, it modulates reward processing in the striatum (Staudinger, Erk & Walter, 2011), and cognitive processes necessary for reward processing (e.g., allocation of attentional resources; Wallis & Kennerley, 2010). The orbitofrontal cortex (OFC) is involved in guiding decision making, alongside the ventromedial PFC (vmPFC) that plays a role in determining expected value of potential rewards and evaluating received reward (Peters & Büchel, 2010; Rushworth, Noonan, Boorman, Walton & Behrens, 2011; Wallis & Kennerley, 2010). Although RST initially proposed the BAS to be located in this 4-structure (VTA, VS, VPal, PFC) network, recent work has proposed the need for the integration of the BAS with the wider body of research on the reward system (Krupic & Corr, 2017). This could incorporate the hippocampus (implicated in reward memory; Lansik, Goltstein, Lankelma, McNaughton & Pennartz, 2009) and amygdala (implicated in reward prediction, learning and reward related arousal; Baxter & Murray, 2002; Murray, 2007) into the structural anatomy of the BAS.

1.3 The Fight Flight Freeze System

The BIS and FFFS are both neurologically organized in a hierarchal structure based on the proximity of the threatening stimulus, called *defensive distance*, but differ in the orientation to the stimulus referred to as *defensive direction* (McNaughton & Corr, 2004). The FFFS has a defensive direction that is orientated away from the potential threat (active avoidance). According to McNaughton & Corr (2004), at the most proximal *defensive distance*, where the most intense active avoidance response is seen, activity is predominately located in the periaqueductal gray (PAG). As defensive distance increases, the pattern of activity shifts to

higher level regions, moving first to the medial hypothalamus, followed by the amygdala, anterior cingulate cortex (ACC) and finally the prefrontal ventral stream at the largest (safest) defensive distance. The PAG is seen as one of the more primal core brain areas (Motta, Carobrez & Canteras, 2017), whose stimulation is related to fight, flight, and freeze behaviours (Assareh, Sarrami, Carrive & McNally, 2016; Deng, Zhao & Wang, 2016). The PAG projects to the medial hypothalamus, which is involved in encoding and retrieving fear memories, as well as responding to threatening stimuli (Gross & Canteras, 2012). In response to threatening stimuli, the hypothalamus acts as a go-between for information passing between the PAG and amygdala, however, it is skipped in response to painful stimuli (Gross & Canteras, 2012; Motta, Goto, Gouveia, Baldo, Canteras & Swanson, 2009). Although often seen as a purely fear related structure, it has also been implicated in processing of primal rewards, suggesting that different distinct areas may be involved in multiple motivation systems (Motta, Carobrez & Canteras, 2017).

The amygdala has long been seen as the central hub for fear processing (Davis, 1992). It has been implicated in fear learning (Kiefer, Hurt, Ressler & Marver, 2015) and organization of immediate and more long-term threat responses (Davis, Walker, Miles & Grillon, 2010). The amygdala mediates threat response through intra-amygdala circuits and projections to other fear circuitry such as the hypothalamus and PAG (Gross & Canteras, 2012; Fox & Shackman, 2019). The ACC has been implicated as a key structure in contextual fear memory and modulating fear expression, which are firmly in the remit of the FFFS (Frankland, Bontempi, Kaczmarek & Silva, 2004; Tang, Ko, Ding, Qiu, Calejesan & Zhuo, 2005; Einarsson & Nader, 2012; Milad, Quirk, Pitman, Orr, Fischl & Rauch, 2007). However, the dorsal ACC has been identified as a

potential conflict monitoring system, which suggests different subregions of the ACC may be attributed to either the BIS or FFFS (Botvinick, Cohen & Carter, 2004).

RST proposes that activity in the prefrontal ventral stream is related to the most complex forms of defensive avoidance at the most maximal defensive distances. Behaviours such as stereotyping (Milne & Grafnam, 2001; Quadflieg et al., 2009), obsession (Apergis-Schoute et al., 2018; Fineberg et al., 2018) and responses to small monetary loss (O'Doherty et al., 2001) can be reflected in the neural activity in the prefrontal ventral stream. However, a review of ventromedial PFC functioning has found it to also be responsible for processing rewards suggesting it is not purely an avoidance-based structure (Oldham et al., 2018). That said, it was stated in the revisions that it does not imply that these areas are solely devoted to defense, just that they are involved in response to distal threat (McNaughton & Corr, 2004).

1.4 The Behavioral Inhibition System

The defensive direction of the BIS is orientated towards the threatening stimuli (passive avoidance behaviour). At the most proximal defensive distance the main areas of activity are the amygdala and septo-hippocampal system. As defensive distance increases to safer levels activity patterns shift to the posterior cingulate cortex (PCC) and finally the prefrontal dorsal stream (Pickering & Corr, 2008). The septo-hippocampal system (SHS), containing the septum and hippocampus, is the key network implicated in the BIS (Gray, 1982). The area was identified in anxiolytic drug studies that found similar effects to hippocampal lesions on animal anxiety behaviours (Gray, 1982). RST proposes that SHS is involved in cognitive aspects of more conventional anxiety and generalized anxiety disorder (McNaughton, 1997), but encodes all types of anxiety (McNaughton & Gray, 2000). The hippocampus has long been accepted as a key structure in cognitive processes, such as memory and learning (Teyler & DiScenna, 1985;

Eichenbaum, 2017; Bird, 2017). This functioning makes it a critical structure within the BIS, due to the mediating role it plays. Indeed, hippocampal dysfunction has been found to impair extinction of avoidance learning, which may lead to persistent avoidance responses seen in anxiety disorders (Cominski, Jiao, Catuzzi, Stewart & Pang, 2014). The revised version of RST, in particular highlights the role of the amygdala in processing both fear and anxiety (LeDoux, 1994; McNaughton & Corr, 2004). More specifically, with regard to BIS, the amygdala is responsible for controlling the level of arousal (McNaughton & Gray, 2000). Sole activation of the amygdala would be characterized as a pure fear response, but simultaneous activation of the SHS and amygdala constitutes an anxiety response (McNaughton & Gray, 2000).

As threat becomes more distal it is proposed activity moves to the PCC. The PCC has been implicated in memory retrieval, planning and controlling attentional focus (Leech & Sharp, 2014). In the RST context, the PCC is proposed to be related to higher order anxieties that lack any simple avoidance strategies, such as agoraphobia or nyctophobia (Corr & McNaughton, 2004). The attribution of the PCC to the BIS is supported by reviews indicating its role in the assessment of potential threat (Fiddick, 2011), a key aspect of the BIS.

At the most distal defensive distances activity is located in the prefrontal dorsal stream. It is proposed that the prefrontal dorsal stream controls high level passive avoidance and risk assessment behaviours and is related to deep forms of obsession and complex forms of anxiety, such as social anxiety (Corr & McNaughton, 2004). Indeed, this is supported by studies finding decreased regional homeogenity in the dlPFC of individuals with social anxiety disorder (Qui et al, 2011). The dlPFC has also been found to influence activity in other brain areas in response to predictable threat, while the dorsomedial PFC (dmPFC) influences activity when processing unpredictable threat (Wheelock, Sreenivasan, Wood, Ver Hoef, Deshpande & Knight, 2014).

1.5 Psychometric evaluation of RST

Although RST started as a bottom-up neurobiological theory of personality, the most widely used method to quantify individual differences in the subsystems of RST is the use of psychometrics (Smillie, 2008). There are currently two streams of psychometric evaluation for RST; scales developed on the basis of the original theory and more recent scales developed considering the revisions to RST. The most widely used original scales are the BIS/BAS scale (Carver & White, 1994) and the Sensitivity to Reward/Sensitivity to Punishment questionnaire (SRSPQ; Tourrubia, Avila, Moltó & Caseras, 2001). These scales were designed to quantify the two systems of the original RST, and thus, do not separate the BIS and FFFS, though attempts have been made to distinguish the systems from items in the BIS/BAS scale (Heym, Ferguson & Lawrence, 2008), which may prove useful in uniting findings from studies that examined original RST with the theoretical changes seen in revised RST. Nevertheless, these original scales are still being widely used since the revisions to RST to classify approach/avoidance tendencies (e.g., Balconi, Angioletti, De Filippis & Bossola, 2019; Sun, Luo, Chang, Zhang, Liu, Jiang & Xi, 2020; Bossola, Angioletti, Di Stasio, Vulpio, De Filippis & Balconi, 2020). More recent scales have been designed based on the revised RST, such as the RST-PQ (Corr & Cooper, 2016), RSQ (Smederevac, Mitrović, Čolović & Nikolašević, 2014), rRST-Q (Reuter, Cooper, Smillie, Markett & Montag, 2015) and the Jackson 5 (Jackson, 2009). Each of these scales separates the BIS and FFFS, allowing for a more theoretically sound measure of RST. However, issues remain in fully encapsulating all RST aspects (see Corr, 2016; Krupić, Corr, Ručević, Križanić & Gračanin, 2016; Walker & Jackson, 2017). The revised scales should be more useful in delineating structures that have distinct and shared roles in different RST systems. For example, the PAG is attributed to the FFFS and has been implicated in instinctual emotional

processes such as defensive responses and fear learning but it also plays a role mediating reward seeking behaviour and goal-oriented responses to more primal rewards such as food, water and drugs which suggests it may be involved in the BAS in some form (see Motta, Carobrez & Canteras, 2017).

1.6 Neuroimaging techniques

There is now a wealth of neuroimaging techniques available to study the brain; from electroencephalogram (EEG) which offers superb temporal resolution (Gui et al., 2010), to Computed Tomography (CT) scans that offer a more structural view of the brain (Jeena & Kumar, 2013). One of the most widely used neuroimaging technique is Magnetic Resonance Imaging (MRI) and functional MRI (fMRI; Glover, 2011). MRI uses gradients in magnetic fields to create images of the brain with great spatial resolution, however, is only useful for examining structure rather than functioning (Glover, 2011). This was overcome by the development of fMRI, which can image regional, time varying changes in the brain by assessing metabolic changes, which are reflective regional activity (Glover, 2011). FMRI offers great spatial resolution but can also offer temporal resolution in the 100ms range (Ogawa et al., 2000). This technique's ability to offer great temporal and spatial resolution makes it an informative tool to examine the proposed neural structures of RST systems and will be the focus of this review.

1.7 Aims & Objectives

The current systematic review has three aims. Firstly, it aims to investigate the relationship between psychometric measures of RST and the theoretically proposed neural circuitry of RST. For both the original and revised psychometrics to be considered as valid measures of individual differences in reinforcement sensitivity, they must be associated with the

neurological systems put forward by the RST. In other words, the scales should be able to discern individual differences in the structure, activation, and connectivity of the proposed systems. Secondly, it aims to identify other areas outside of the proposed neural circuitry of RST that may need to be incorporated into the theoretical framework of reinforcement sensitivity. Finally, it aims to provide recommendations for future studies that examine the neural correlates of RST – in terms of methodological considerations and theoretical implications.

2. Method

2.1: Research Strategies

The literature search was conducted in four international electronic databases: Scopus, PsychInfo, Web of Science and PubMed. From this cohort only peer-reviewed full-text journal articles written or published in English were included. The research was restricted to studies conducted on healthy adult samples with no restrictions regarding gender or ethnicity. The search terms aimed to capture all studies that used certain forms of neuroimaging (MRI, fMRI, EEG, MEG) alongside a psychometric evaluation of either original or revised RST. The search was conducted in November 2019. The search of the database was conducted using the following search terms:

"Reinforcement Sensitivity" OR "Behavioural Activation" OR "Behavioural Approach" OR "Behavioural Inhibition" OR ("fight" AND "flight") OR "BAS" OR "BIS" OR "FFFS" OR "FFS" OR "Punishment Sensitivity" OR "Reward Sensitivity" AND "neural" OR "biobehavioural" OR "neuropsychology" OR "neuroimaging" OR "Magnetic resonance imaging" OR "MRI" OR "functional magnetic resonance imaging" OR "FMRI" OR

"Electroencephalography" OR "Event Related Potentials" OR "Event-Related Potentials" OR "ERP" OR "magnetoencephalography" OR "MEG".

An updated search was performed in April 2021 to account for studies that had been published between 2019-2021 and to account for the initial use of the English spelling of "behavioural" instead of the more widely used American spelling of "behavioral". This search found 20042 studies which was reduced to 5338 studies after duplicate removal and accounting for the results of the original search. This led to the inclusion of 3 extra fMRI-based studies that were published after the initial search. There were no additional studies found due to changing the search terms to American spelling.

2.2: Eligibility Criteria

The results of the systematic review were examined by two researchers (first and second authors - both PhD students). Results were first checked for duplicates, with any duplicates being removed. Title and Abstracts were then scanned for inclusion based on the following criteria: (i) Contained a neuroimaging technique (e.g., MRI, fMRI, EEG), which led to the exclusion of studies that may have discussed neural structures but did not directly use neuroimaging; (ii) Included a psychometric assessment based on RST (e.g., BIS/BAS, RST-PQ, SRSPQ), which led to the exclusion of studies using only potentially related psychometric scales (e.g., impulsivity, extraversion, neuroticism), but not those that included at least one direct measure of RST; (iii) Explicitly examined RST in relation to the neuroimaging data, which led to the exclusion of studies that have collected neuroimaging data and psychometric data, but did not directly compare them; (iv) Contained a healthy adult sample, which led to the exclusion of studies on

adolescents and individuals with various disorders (e.g., alcohol disorder); (v) The papers were available in English language format, which may have led to the exclusion of relevant papers that were not available in English.

The exclusion of studies based on title and abstract were completed independently by both researchers, and subsequently included papers were compared and discussed to make sure no relevant papers were omitted. After the researchers reached agreement of inclusion of research, the body of research was split into two separate reviews - the current on research investigating MRI and fMRI, and a second one on investigation into research investigating EEG and ERP (reported elsewhere; Reference anonymized for review process). Each researcher performed an in-depth examination of the content of their relevant research and excluded any papers that did not meet the eligibility criteria. Data were then extracted, with each researcher reviewing a subsample of the other's papers to maintain consistency and correct procedure. Therefore, the current study focuses on relevant MRI (structural and functional) literature only.

2.3: Quality assessment

The 20-item AXIS assessment tool was used as part of quality assessment (Downes, Brennan, Williams, & Dean, 2016). Each study was assessed individually and assessed a score out of 20. The AXIS rates the papers on a wide number of factors related to methods, sample, and reporting. Previous research has used cutoff points of 0-7 for low quality papers, 8-15 for medium quality papers and 15+ for high quality papers (Wallace, Heym, Sumich & Fido, 2020). All studies in this review were deemed as high-quality papers based off their AXIS score being greater than 15.

2.4: Data selection

Table 1 shows all the data included in this review.

Table 1: *Details of studies included in the systematic review*

***** Insert Table 1 about here******

3: Results

3.1: Study selection

The below PRISMA flow chart provides an accurate summary of the articles identified, screened, and finally included in this paper (Figure 1; Moher, Liberati, Tetzlaff, Altman & The PRISMA group, 2009). It also breaks down the split of studies for the current MRI systematic review and its sister EEG systematic review (reported elsewhere; Reference anonymized for review process).

******Insert Figure 1 here**********************************

Figure 1: PRISMA flow chart of selection process

3.2: Structural studies looking at grey matter volume (GMV)

Seven studies examined GMV, with 5 studies using the SRSPQ (Tourrubia, Avila, Moltó & Caseras, 2001) and 2 using the BIS/BAS scales (Carver & White, 1994) to assess RST. Of the studies using the SRSPQ, 2 studies found a positive correlation between sensitivity to punishment (SP) and GMV in the right hippocampus (Barros-Loscertales et al., 2006a; Levita et al., 2014) with the study looking at an all-male sample finding also positive correlations with GMV in the parahippocampus and amygdala (Barros-Loscertales et al., 2006a). One other study supported the positive correlation between SP and GMV in the amygdala in males, but not

females (Adrian-Ventura et al., 2019). Three studies investigated sensitivity to reward (SR). One study, using an all-male sample, found a negative correlation with GMV in the caudate, putamen, superior frontal cortex and globus pallidus (Barros-Loscertales et al., 2006a). Another study also found a negative correlation between SR and GMV in the left caudate (Parcet et al., 2020). The final study that investigated SR found a negative correlation with GMV in the ACC, the medial and left lateral PFC, left and superior temporal lobe and the left insula for both genders, and in the NAcc and left caudate for males only (Adrian-Ventura et al., 2019b). Of the studies using the BIS/BAS scales, BIS was found to be positively correlated with GMV in the hippocampus in one study (Cherbun et al., 2008). The other study found BIS to be negatively correlated with GMV in the parahippocampus and BAS to be positively correlated with GMV in the vmPFC and inferior parietal lobe for females, but an exactly opposite pattern for males (Li et al., 2014).

3.3: Resting state connectivity and other resting state studies

Three studies investigated BAS-related traits and resting state connectivity. One study found a positive correlation between SR and ACC-vmPFC and vmPFC-VTA connectivity (Adrian-Ventura et al., 2019). One study found a positive correlation between BAS and left-right striatum and right frontal gyrus-right striatum connectivity (Dong et al., 2018). One study found a positive correlation between BAS-Fun Seeking and OFC-putamen connectivity and a negative correlation between BAS-Drive and middle cingulate cortex-caudate connectivity (Angelides et al., 2017).

Four studies looked at other resting state measures. A positive correlation was found between SR and the hurst component in the VS and OFC (Hahn et al., 2012). A negative correlation was found between SP and regional homogeneity in the amygdala and hippocampus (Hahn et al., 2013). A positive correlation was found between BAS-Fun Seeking and fractional anisotropy in

the left corona radiata and superior longitudinal fasciculus and with diffusivity in the left inferior longitudinal fasciculus and the inferior fronto-occipital fasciculus (Xu et al., 2012). Finally, a negative correlation between BIS and the number of white matter fibres in corpus callosum , the fibre density in the unicate fasciculus and the number of fibres in the right and left accumbofrontal tracts (Park et al., 2021).

3.4: Monetary incentive-based tasks

Twelve studies used monetary incentives in their tasks. Of these, 8 studies included an examination of brain activation during a monetary incentive delay (MID) task in relation to RST Four studies found a positive correlation between SR scores and activity in the VS during reward processing (Costomero et al., 2013a; Hahn et al., 2009; Hahn et al., 2011), and the BAS scale (Simon et al., 2010). This was further supported by three studies using other money-based tasks, with two finding a positive correlation between the BAS scale and activity in the VS while processing reward (Dong et al., 2018; Eryilmaz et al., 2017), and one specifically for the BAS-Drive subscale (Customero et al., 2016). A positive correlation was found between activity in the medial OFC and SR (Hahn et al., 2009) and BAS scores (Simon et al., 2010) when processing rewards. One study found a positive relationship between SR and activity in the left midbrain when processing reward (Costomero et al., 2013a). One study found a negative correlation between SR and midbrain-OFC connectivity during incentive processing and SR and NAcc-left amygdala connectivity during reward anticipation (Costomero et al., 2013a). A positive correlation between SR and activity in the DMN and right FPN during anticipation of rewards and punishments (Costumero et al., 2015). Finally, one study found a positive correlation between SR and activity in both the PCC and precuneus in men when comparing dollar wins to no win (Dingra et al., 2021).

Regarding BIS/FFFS traits, SP was found to be positively correlated with amygdala-hippocampus connectivity during loss anticipation by 2 studies (Hahn et al., 2010; Hahn et al., 2013). However, the 45 participants used in the 2010 study were also used in the 89 participant study from 2013, which may explain the repeated findings. One study found and a negative correlation between BIS and activity in the VS when receiving reward (Simon et al., 2010). Another study found a negative correlation between SP and activity in the right middle frontal and postcentral gyri for women when comparing dollar wins to no win conditions as well as a negative correlation between SP and activity in the right anterior insula, left superior frontal gyrus and right temporal gyrus for women only (Dingra et al., 2021).

3.5: Affective picture-based tasks

Six studies investigated the relationship between RST and brain activity when viewing affective pictures. For BAS traits, a positive correlation was found between SR and activity in frontal areas such as the OFC (Customero et al., 2013b) and the medial PFC (Barros-Loscertales et al., 2010), but negatively with activity in the superior frontal gyrus when viewing erotic images (Barros-Loscertales et al., 2010). Positive correlations were also found for SR and activity in the right occipital gyrus, precuneus (Barros-Loscertales et al., 2010), the left insula and left VS (Customero et al., 2013b) when viewing erotic images. BAS was found to have a positive correlation with activity in the left hippocampus/parahippocampus (Reuter et al., 2004) and with modulation of the FPN, but a negative correlation with modulation of the DMN when viewing erotic images (Costumero et al., 2015). One other study looked at positive valence and found a significant difference between high and low BAS groups, with high BAS individuals showing greater activation in the middle cingulate cortex, right NAcc, right precuneus, superior orbital/medial gyrus and middle temporal gyrus (Radke et al., 2016). One study found SR was

found to be negatively correlated with activity in the right lateral PFC and left occipital cortex when viewing aversive images (Barros-Loscertales et al., 2010).

Only one study looked at BIS in relation to erotic images and found a positive correlation with the activity in the left ACC, thalamus, right amygdala, insula, left basal ganglia, left brain stem & PCC, with a negative correlation with activity in the right OFC (Reuter et al., 2004). A positive correlation was found between BIS and activity in the ACC, PCC and thalamus for fear evoking and disgusting stimuli, as well as a positive correlation with activity in the amygdala for fear evoking images (Reuter et al., 2004). Finally, one study split groups into high and low BIS conditions and found greater activation in the dlPFC to angry faces and greater activation of the right dorsal ACC to fearful faces for the high BIS condition (Bunford et al., 2017).

3.6: Food related tasks

Four studies used food related tasks. Van Rijn et al., (2016) examined the association between RST and neural activity in the sating of hunger. They found that for those in the hunger condition, activity in the VS (specifically the caudate), amygdala and ACC correlated negatively with BAS-Drive when receiving calories. For those in the sated condition BAS-Drive was positively correlated with activity in the left caudate. One study found a positive correlation between BAS-Drive and activity in the left OFC, right VS amygdala, VTA and VPal and between BAS-Reward responsiveness and activity in the OFC and VPal when viewing appetizing food images compared to bland food images. They also found a positive correlation between BAS-Drive and activity in right OFC and right VS when viewing disgusting food images compared to bland (Beaver et al., 2006). One food related study used sweets as a reward in a card guessing game with high and low rewards and losses (Luking et al., 2013). BAS was positively correlated with activity in the inferior frontal gyrus in low loss trials, and with activity

in the right caudate and the right lateral OFC when comparing low loss trials to neutral trials. However, these same regions were negatively correlated with BAS when comparing higher loss to lower loss trials. Neseliler et al., (2017) examined neural responses to high and low-calorie food during exam and non-exam periods. They found BIS was negatively correlated with connectivity between the vmPFC and dlPFC but positively correlated with activity in the vmPFC and amygdala when comparing the exam condition to the non-exam condition for high-calorie images compared to low-calorie images.

3.7: Go/No-Go tasks

Two studies investigated the association neural responses to Go/No-Go tasks and the SR scale of the SRSPQ (Funetas-Claramonte et al., 2016a; Funetas-Claramonte et al. 2016b). The first study found SR correlated with increased activity in the inferior frontal gyrus for No-Go and infrequent Go trials compared to frequent Go trials (Funetas-Claramonte et al., 2016a). The second study used a stop signal variation of the Go/No-Go task (Funetas-Claramonte et al., 2016b), showing a negative correlation between SR and the left fronto-parietal network and the anterior DMN for stop error trials. SR also had a positive correlation with activity in a cluster containing the bilateral precentral and postcentral gyri, the superior parietal cortex, the bilateral supplementary motor area, and the right cerebellum in stop error trials. SR had a negative correlation with the midline network (containing the ACC and supplementary motor area, the bilateral middle and superior frontal gyri, the bilateral inferior parietal cortex, including the supramarginal gyrus, and the bilateral insula) for successful stop trials.

3.8: N back tasks

Two studies looked at neural responses to an N back task using the BIS/BAS scale. The first study used a 3 back task while pre-exposing the participants to pleasant, unpleasant, and neutral videos (Gray & Braver, 2002). BAS was negatively correlated with activity in the caudal ACC and the posterior rostral ACC for the average of all affective states. When broken down into affective states, BAS was negatively correlated with activity in the caudal ACC for all emotions and BIS was positively correlated with activity in the caudal ACC for pleasant stimuli. When controlling for task related activity in the neutral condition, BIS was positively correlated with activity in the caudal ACC for pleasant stimuli, BAS was negatively correlated with caudal ACC activity in the unpleasant condition. Gray et al. (2005) built on this study by examining a wider array of brain areas on a larger participant pool. They only looked at neutral affective states in their analysis. They found that BAS was negatively correlated with item-related activity in the dorsal ACC, the bilateral PFC, and the bilateral parietal cortex. BAS was positively correlated with state-related activity in the right parietal cortex. BIS was positively correlated with state-related activity in the rostral ACC.

3.9: Switching tasks

Two studies investigated task switching paradigms using the SR subscale of the SRSPQ. In an all-male sample, Avila et al., (2012) found a positive correlation between SR scores and set switching neural activation in the right VS and right inferior frontal cortex, and a negative correlation between SR and activation in the rostral ACC. Funetas-Claramonte et al., (2015) found a negative relationship between SR and neural activity in the inferior frontal gyrus, dlPFC, the ACC, the inferior parietal cortex and postcentral gyrus, and a positive relationship between SR and activity in the posterior cingulate cortex in switch versus repeat contrasts. They also found a negative relationship between left VS activity and SR during switch cues.

3.10: Priming tasks

Two tasks investigated neural activity in response to priming tasks. Mortensen et al., (2015) looked at an all-female sample using a combination of the SRSPQ and neuroticism scales to target all three RST systems. They used SR for BAS, SP for the FFFS and neuroticism for BIS. SR scores were positively associated with activity in the left posterior hippocampus and parahippocampal gyrus for all contrasts, but only in the left caudate nucleus and NAcc in response to valid and invalid targets, in the right OFC and left thalamus in response to cues and valid targets, and in the right caudate nucleus in response to cue primes only. They then used SR scores adjusted by either SP (SR/SP) or N (SR/N) scores to examine the joint subsystems hypothesis. SR/SP and SR/N with activity in the left VS, bilateral OFC and left thalamus for all contrasts. For SR/SP, peak activity was located anterolaterally in the caudate and spread into the NAcc and putamen, and correlated with activity in the left posterior hippocampus, parahippocampal gyrus, fusiform cortex, right lateral occipital cortex and left opercular cortex. SR/N activity peaked posteromedially in the VS, spreading only to the NAcc, and was also associated with activity in the bilateral inferior temporal gyrus, left middle temporal gyrus, right inferior and middle frontal gyrus, and the bilateral OFC. Examining left VS activity, SR was positively, whereas SP and N were negatively correlated. Straumen et al., (2012) found no association between BIS/BAS scale and neural activity in response to a priming task that masked words from participants' prevention and promotion goals.

4. Discussion

4.1: The proposed neural structure of the BAS

RST proposes the BAS is located in a dopaminergic system consisting of the PFC, VS, VPal and VTA (Gray & McNaughton, 2000). This review has found psychometric measures of BAS to be associated with activity in the PFC (Barros-Loscertales et al., 2010; Funetas-Claramonte et al., 2015; Gray et al., 2005), and more specifically the OFC (Hahn et al., 2009; Simon et al., 2010; Customero et al., 2013a; Customero et al., 2013b; Luking et al., 2013; Mortensen et al., 2015). There was also some evidence of structural and resting state differences in the PFC in relation to BAS trait measures (Adrian-Ventura et al., 2019b; Hahn et al., 2012; Li et al., 2014). The involvement of the VS as a BAS structure was consistently supported by correlations with task related activity (Customero et al., 2013a; Customero et al., 2013b; Customero et al., 2016; Hahn et al., 2009; Hahn et al., 2011; Simon et al., 2010; Dong et al., 2018; Eryilmaz et al., 2017; Radke et al., 2016; Van Rijn et al., 2016; Mortensen et al., 2015) and structural and resting state differences (Adrian-Ventura et al., 2019b; Hahn et al., 2012; Barros-Loscertales et al., 2006a; Parcet et al., 2020). BAS was also found to be related to connectivity between the right and left striatum and right frontal gyrus and right striatum (Dong et al., 2018). However, there were limited of findings in regards to the VPal and VTA. One study found a relationship between BAS-Drive and activity in the VTA and VPal and BAS-reward responsiveness and activity in the VPal (Beaver et al., 2006). Another study found a relationship between BAS and GMV of the nearby structure, the globus pallidus (Barros-Loscertales et al., 2006a). The VTA was also found to be related to BAS traits in terms of its connectivity to the vmPFC (Adrian-Ventura et al., 2019ba). Although there was relatively little support for an association between trait BAS and the VPal and VTA, they are critical in reward processing and motivation (Smith, Tindell, Aldridge & Berridge, 2008; Haber & Knutson 2010) and are undoubtedly part of the neural make-up of the reward system. As the BAS is fundamentally a reward processing system it

seems unlikely that the VTA and VPal are not part of the system. It may be that the BAS psychometrics do not effectively isolate the individual differences in the sensitivities of these systems or the tasks do not adequately activate each processing stage of the BAS.

4.2: The proposed neural structure of the BIS and FFFS

This review only found studies that used measures of the original RST, though one study tried to account for a 3-system hypothesis by using a neuroticism measure as index for BIS in addition to the SPSRQ as proposed indices for FFFS and BAS (Mortensen et al., 2015). Therefore, BIS and FFFS have to be evaluated here together rather than as separate structures. At maximal defensive distances, RST proposes BIS activity is located in the prefrontal dorsal stream and FFFS is located in the prefrontal ventral stream (Corr & McNaughton, 2004). This is partially supported by findings that BIS was related to greater activation of the dlPFC when viewing angry faces (Bunford et al, 2017), and in the vmPFC when viewing high calorie food images in addition to reduced dlPFC-vmPFC connectivity (Neseliler et al., 2017). As defensive distance shortens BIS activity moves to the PCC and FFFS activity moves to the ACC (Corr & McNaughton, 2004). Accordingly, both the PCC and ACC were related to BIS when viewing disgusting and fear evoking images (Reuter et al., 2004), and latter also when processing fearful faces (Bunford et al., 2017), performing a standard N back task (Gray et al., 2005) and an N back task after watching a pleasant video (Gray & Braver, 2002). Although it was expected that ACC activity would be associated with BIS/FFFS it is surprising that this is seen in response to pleasant stimuli; however, the authors were cautious about interpreting these findings due to power issues (Gray & Braver, 2002).

In line with the proposition of the septohippocampal system as the main system underpinning the BIS, hippocampal structure was associated with BIS measures (Barros-Loscertales et al., 2006a;

Cherbun et al., 2008; Li et al., 2014; Hahn et al., 2013); however, this was not seen for hippocampal functioning. In terms of the involvement of the amygdala, original BIS trait measures were associated with task related activity (Hahn et al., 2010; Hahn et al., 2013; Reuter et al., 2014), resting state measures and structure of the amygdala (Adrian-Ventura et al., 2019b; Barros-Loscertales et al., 2006a; Hahn et al., 2013). For BIS specifically, the amygdala is proposed to modulate the arousal in the SHS (McNaughton & Gray, 2000). This is supported by studies linking BIS to amygdala-hippocampus connectivity during monetary loss (Hahn et al., 2010; Hahn et al., 2013). The hypothalamus and PAG are the main structures proposed for FFFS, however, the review did not identify any studies showing this relationship with either activity or structure of these systems. There were some findings associating BIS/FFFS traits with activity in the nearby thalamus when viewing erotic, disgusting and fear evoking (Reuter et al., 2004). The authors argued that this discrepancy may be due to difficultly directly applying a theory built of the back of animal literature to human subjects with far more complicated brain structures. On the other hand, the lack of findings may also simply be due to limitations in the literature in terms of sole psychometric assessment of the original systems that conflate BIS and FFFS, highlighting the urgent need to examine BIS and FFFS related functional and structural underpinnings using revised RST scales.

4.3: Potential additional structures for RST systems

This review has identified some common findings of relationships between RST scales and structures outside the initially proposed circuitry. BAS was associated with hippocampal functioning during priming tasks and when viewing erotic pictures (Mortensen et al., 2015; Reuter et al., 2004). The hippocampus is not included in the proposed RST circuitry for the BAS (Gray & McNaughton, 2000); however, it has been implicated in reward memory in the general

559 reward literature (Davidow, Foerde, Galván & Shohamy, 2016 ; Lansik, Goltstein, Lankelma,
560 McNaughton & Pennartz, 2009). It has been argued that reward prediction is modulated by
561 dopamine firing at cortical-striatal synapses, with greater firing for unpredicted rewards and a
562 reduction in firing when reward is omitted (Pickering & Corr, 2008). If the BAS is responsible
563 for reward prediction, then it must first have access to previous data. The hippocampus is widely
564 known for its role in memory (Eichenbaum, 2017; Bird, 2017), so its role in the BAS as the hub
565 for reward memories seems likely. The hippocampus is part of the proposed BIS circuitry, so it
566 may be that the BAS accesses and updates its reward memories from within the BIS structure,
567 with the BIS facilitating BAS related reward processing under certain prediction conditions.

568 Some studies found a relationship between BAS traits and increased activity in the insula when
569 viewing erotic images (Customero et al., 2013b; Rueter et al., 2004) and disgusting images
570 (Rueter et al., 2004) but reduced activity during Go/NoGo tasks (Funetas-Claramonte et al.,
571 2016). BAS was also related to reduced GMV (Adrian-Ventura et al., 2019b). The insula has
572 been implicated in reward prediction (Furl & Averbeck, 2011; Sescusse, Caldú, Segura &
573 Dreher, 2013) and is connected through dopaminergic neurons to the VS indicating a potential
574 role within the BAS (Sescusse, Caldú, Segura & Dreher, 2013). Insula activity increases during
575 sexual arousal (Kühn & Gallinat, 2011), and BAS is related to greater sexual arousal responses
576 (Customero et al., 2013b). However, the insula is widely regarded as a hub for risk management
577 and processing negative stimuli (Knutson & Bossaerts, 2007; Wright, He, Shapira, Goodman &
578 Liu, 2004). The relationship between BAS and insula activity to disgusting images is surprising
579 due to the appetitive nature of the BAS and should be examined further (Reuter et al., 2004).
580 However, the idea that the BAS and approach motivation is associated with only positive affect
581 has been challenged by research indicating its role in anger (Harmon-Jones, 2003).

BAS traits were associated with reduced activity in the ACC (Van Rijn et al., 2016; Funetas-Claramonte et al., 2016; Gray & Braver, 2002; Gray et al., 2005) and with increased connectivity between the ACC and vmPFC (Adrian-Ventura et al., 2019a). The research suggests that the relationship between BAS and ACC represents cognitive control and efficiency, rather than emotion processing (Gray & Braver, 2002; Gray et al., 2005), so its potential addition to the BAS circuitry may not be justified.

4.4: Sex differences

Although most cohorts included both males and females, few controlled for sex differences or directly investigated them. Two structural studies investigated sex as a variable in their analysis, one study found differences in the GMV of the amygdala was related to BIS measures and the GMV of the NAcc was related to BAS measures, but only in males, with no relationship found for females (Adrian-Ventura et al., 2019b). Another study found a negative association between BIS and GMV in the parahippocampus and positive association between BAS and GMV in the vmPFC and inferior parietal lobe for females, but the exact opposite pattern was found in males (Li et al., 2014). Finally, one study examined gender differences in a MID task and different patterns of activity for men and women related to both SP and SR (Dingra et al., 2021). These studies highlight how the relationship between RST traits and brain structure and function may differ between the sexes. Indeed, this is supported by general trends in brain structure and functioning that indicate sex differences. Males tend to have greater overall brain volume with a higher percentage of white matter, but a lower percentage of gray matter, whilst females have a greater cerebral blood flow than males. Moreover, sex-specific differences in dopaminergic, serotonergic, and GABAergic functioning indicate that male and female brains are neurochemically distinct (Cosgrove, Mazure & Stanley, 2007). This is further supported by

psychometric studies finding sex differences in RST traits (Corr & Cooper, 2016; Heym, Ferguson & Lawrence, 2008; Tull, Gratz, Latzman, Kimbreal & Lejuez, 2010), although these differences were often not big enough to justify splitting the data by sex. Due to differences in neuroimaging and psychometric data between males and females, future studies should always include sex as part of their analysis to ascertain exactly how RST functioning differs between sexes.

4.5: Limitations of psychometric evaluation

The psychometrics used by the studies in this review leads to several limitations that need to be addressed by future work. Firstly, all the studies included in this review were flawed in their ability to examine the current conceptualization of RST due to the sole use of scales assessing original RST. The only scales that were identified by this review were the BIS/BAS scale and SRSPQ. Both scales were designed in the light of original RST theory, which did not separate the BIS and FFFS. These systems were revised and delineated over 20 years ago, based on a wealth of research that identified anxiety and fear as separate constructs (Gray & McNaughton, 2000). One study did attempt to address this by using a neuroticism scale to index BIS and the SP scale to index FFFS (Mortensen et al., 2015). However, neuroticism cannot be considered a direct measure of BIS given its 30-45-degree rotation away from BIS (Pickering, Corr & Gray, 1999). Similarly, although some argue SP is more representative of FFFS (Mortensen et al., 2015), it is generally viewed as a conflation of both systems (Corr, 2016). Finally, there are more psychometrically robust methods to assess BIS and FFFS as separate constructs that have been specifically developed to delineate these in line with the revised theory, such as the RST-PQ (Corr & Cooper, 2016), the RSQ (Smederevac, Mitrović, Čolović & Nikolašević, 2014) and the rRST-Q (Reuter, Cooper, Smillie, Markett & Montag, 2015). It is crucial that future

neuroimaging studies include a measure of revised RST to allow an examination of the BIS and FFFS as separate systems. The continued conflation of these two systems, due to an overreliance on the well-established original RST scales, severely limits our understanding and the scientific progression of RST.

Secondly, many studies opted to only use one subscale depending on the task (e.g., BAS scale for reward paradigms, BIS/FFFS for punishment paradigms). Although it may seem appropriate as the BAS is activated by appetitive stimuli and the FFFS by aversive stimuli, it does not allow for examination of the mediating role of the BIS. The BIS is responsible for mediating all goal conflicts, whether that be a classic approach/avoidance conflict or more complex conflicts such as conflicts between multiple rewards or punishments. Many of the tasks expected to only activate one system, would inherently activate the BIS as well. For example, the MID task is often used in either a solely gain or solely loss context but will often have differing levels of gain or loss. A MID task looking at small, large or no gains may not activate the FFFS, but would activate the BAS and BIS due to reward-reward conflicts. The use of single subscales is also holding back the theoretical advancement of RST. Original RST proposed that each of the subsystems were separable, in other words the sensitivities in each system are uncorrelated with the other systems. However, according to a joint subsystems hypothesis (JSH; Corr, 2002; Smillie, Pickering & Jackson, 2006), the systems are inter-dependent, with the output of the BAS and BIS being moderated by the sensitivities of the other systems, though, the FFFS output is only affected by the FFFS sensitivity (Smillie, Pickering & Jackson, 2006). Future studies should strive to test these assumptions by including all subscales in their analysis. However, it should also be noted that psychometric measures of RST may measure the functional outputs of each

system rather than their sensitivities (Pickering, 2008). As the JHS proposes that it is the sensitivities of each system that modulates the output of the other systems, currently developed scales may not be adequate for examining the JHS (Smillie, Pickering & Jackson, 2006).

A final issue with the psychometric measures used by some studies in this review comes in the form of classifying individuals as high and low on the trait measures. Possibly due to the slow uptake of revised scales of RST, and the number of competing revised RST scales, there is no standardized scoring or cut-off for classifying individuals as high or low in each trait. For example, Bunford et al., (2017) used a median split on BIS scores to form high and low BIS groups. However, by using a median split, participants can be classed as either high or low based on a difference of 1 score. Establishing normative scores and considering systems for cut-offs (e.g., 2 SDs above or below the mean or simple slope analysis) would provide more certainty on whether an individual falls into a high or low reinforcement sensitive group. This issue is exemplified by Radke et al., (2106), where using a median split resulted in a high BAS group with a mean score of 35.9 and a low BAS group with mean score of 31.1 - both of these group means fall in the highest 33% of possible scale scores and labelling latter as low BAS is questionable to say the least. It is advised that continuous psychometric data is not artificially split unless there is strong justification to do so, such as comparing extreme groups that may be of greater interest, and even this must be done cautiously (DeCoster, Gallucci & Iselin, 2011).

4.6: Limitations of task selection

The tasks used to examine RST in this review suffer from paradoxically being too simple while simultaneously being too complex. There are 3 main goals that tasks assessing RST should be able to achieve. Firstly, they should be able to attempt to activate each system individually without interference from the other systems so that each individual system can be examined.

Secondly, they should be able to activate all systems simultaneously to examine how the systems interact with each other. Finally, they need to have enough depth that they simulate the whole spectrum of defensive distance, not just the most distal levels.

A task that can activate each system separately must avoid any conflict that may activate the BIS (McNaughton & Corr, 2004). As previously mentioned, some studies looked at MID tasks as only activating one system, such as gain MID tasks only activating BAS. However, using rewards that vary in size the BIS would be active to mediate approach-approach conflicts. To activate each system separately tasks would require various levels. To individually activate the BAS the task would need to offer a reward schedule where, regardless of strategy, the participant would gain a consistent reward with no chance of losing this reward. To activate the FFFS, the task would need to have a single consistent threat where there is no chance of reward or conflict between avoiding multiple threats. There may be more difficulty in solely activating the BIS, due to its role as a mediation system. Conceptually, the BIS may only be activated when a conflict arises. This means activation of the BIS entails activation of either the BAS or FFFS first. However, this could potentially be overcome by creating a task where the outcome of the participants actions remains ambiguous until the end of the task. This ambiguity may allow for BIS activation while keeping BAS and FFFS involvement minimal. Theoretically the BIS inhibits all behaviours until it resolves goal conflict and lets one system gain dominance to achieve the optimum outcome. In a fully ambiguous task, there would be no clear optimal strategy so only the BIS should be activated trying to solve this impossible problem. Most tasks in this review are successful in generating some form of conflict, such as conflicts arising in the MID tasks mentioned earlier; however, none of the tasks used exhaustively examine or manipulate all the possible conflicts. To provide a deeper examination of RST in terms of human

behaviour and neurobiology these tasks should strive to manipulate different intensities of conflicts including both within and between system conflicts.

Finally, tasks need to have the ability to activate every level of the neural structures included in the RST systems. Brain activity in the FFFS and BIS is structured in a hierarchical fashion based on defensive distance (Gray & McNaughton, 2000). Using monetary loss to trigger FFFS and BIS activity are likely to show activity only in the higher regions of the hierarchy as they are not sufficiently aversive. To stimulate deeper regions may require some form of pain stimuli (Roy et al.,2014). Using punishments such as aversive sound blasts or electric shocks would trigger deeper activity in the amygdala and PAG. Indeed, fMRI can be compatible with tactile stimulation such as air puffs that could be used as a negative event (e.g., Kumari et al., 2007)

4.7: Limitations of this review

This review provides an overview of associations between RST scales and (f)MRI correlates, broken down by different tasks. It has made recommendations on the use of psychometric scales and task selection to help guide future research to appropriate methods for assessing neural correlates of RST in light of its revisions. What this review has not focused on are the inter-study variations in (f)MRI methodology. The studies identified varied on a number of levels such as image acquisition, image pre-processing, data analysis and the scanner used, which may impact findings and interpretations drawn. Future work could address these issues by performing an in-depth analysis to take these aspects into account, which may add to the current picture and further our understanding of the neural correlates of RST.

4.8: Conclusion

In conclusion, the original RST measures of BIS and BAS seem to map onto some of the proposed circuitry. There was strong support for the role of the PFC and VS in the BAS circuitry, but less evidence regarding the VPal and VTA. It was not possible to examine the BIS and FFFS separately as all the studies in this review used an original RST scale. Nevertheless, there is evidence for some of the structures related to larger defensive distances such as the PFC and cingulate cortices, but no evidence for deeper structures activated at the most proximal distances (e.g., PAG). Future studies need to adopt the use of revised RST scales, diversify the tasks used so they can target the whole spectrum of defensive distance and simplify tasks to isolate each system so their neural underpinnings can be more precisely delineated.

References

Adrián-Ventura, J., Costumero, V., Parcet, M. A., & Ávila, C. (2019). Linking personality and brain anatomy: a structural MRI approach to Reinforcement Sensitivity Theory. *Social cognitive and affective neuroscience*, *14*(3), 329-338.

Adrián-Ventura, J., Costumero, V., Parcet, M. A., & Ávila, C. (2019). Reward network connectivity "at rest" is associated with reward sensitivity in healthy adults: a resting-state fMRI study. *Cognitive, Affective, & Behavioral Neuroscience*, *19*(3), 726-736.

Angelides, N. H., Gupta, J., & Vickery, T. J. (2017). Associating resting-state connectivity with trait impulsivity. *Social cognitive and affective neuroscience*, *12*(6), 1001-1008.

Apergis-Schoute, A. M., Bijleveld, B., Gillan, C. M., Fineberg, N. A., Sahakian, B. J., & Robbins, T. W. (2018). Hyperconnectivity of the ventromedial prefrontal cortex in obsessive-compulsive disorder. *Brain and neuroscience advances*, *2*, 2398212818808710.

Arias-Carrión, O., Stamelou, M., Murillo-Rodríguez, E., Menéndez-González, M., & Pöppel, E. (2010). Dopaminergic reward system: a short integrative review. *International archives of medicine*, *3*(1), 1-6.

Assareh, N., Sarrami, M., Carrive, P., & McNally, G. P. (2016). The organization of defensive behavior elicited by optogenetic excitation of rat lateral or ventrolateral periaqueductal gray. *Behavioral neuroscience*, *130*(4), 406.

Avila, C., Garbin, G., Sanjuán, A., Forn, C., Barrós-Loscertales, A., Bustamante, J. C., ... & Parcet, M. A. (2012). Frontostriatal response to set switching is moderated by reward sensitivity. *Social cognitive and affective neuroscience*, *7*(4), 423-430.

Balleine, B. W., Delgado, M. R., & Hikosaka, O. (2007). The role of the dorsal striatum in reward and decision-making. *Journal of Neuroscience*,*27*(31), 8161-8165.

Balconi, M., Angioletti, L., De Filippis, D., & Bossola, M. (2019). Association between fatigue, motivational measures (BIS/BAS) and semi-structured psychosocial interview in hemodialytic treatment. *BMC psychology*, *7*(1), 49.

Barrós-Loscertales, A., Meseguer, V., Sanjuán, A., Belloch, V., Parcet, M. A., Torrubia, R., & Ávila, C. (2006). Behavioral inhibition system activity is associated with increased amygdala and hippocampal gray matter volume: a voxel-based morphometry study. *Neuroimage*, *33*(3), 1011-1015.

Barrós- Loscertales, A., Meseguer, V., Sanjuán, A., Belloch, V., Parcet, M. A., Torrubia, R., & Avila, C. (2006). Striatum gray matter reduction in males with an overactive behavioral activation system. *European Journal of Neuroscience*, *24*(7), 2071-2074.

761 Barrós-Loscertales, A., Ventura-Campos, N., Sanjuán-Tomás, A., Belloch, V., Parcet, M. A., &
762 Ávila, C. (2010). Behavioral activation system modulation on brain activation during
763 appetitive and aversive stimulus processing. *Social Cognitive and Affective*
764 *Neuroscience*, *5*(1), 18-28.

765 Baxter, M. G., & Murray, E. A. (2002). The amygdala and reward. *Nature reviews neuroscience*,
766 *3*(7), 563-573.

767 Beaver, J. D., Lawrence, A. D., Van Ditzhuijzen, J., Davis, M. H., Woods, A., & Calder, A. J.
768 (2006). Individual differences in reward drive predict neural responses to images of food.
769 *Journal of Neuroscience*, *26*(19), 5160-5166.

770 Bird, C. M. (2017). The role of the hippocampus in recognition memory. *Cortex*, *93*, 155-165.

771 Blanchard, R.J. and Blanchard, D.C. (1990a) 'An ethoexperimental analysis of defense, fear and
772 anxiety', in N. McNaughton and G. Andrews (eds), *Anxiety*. Dunedin: Otago University
773 Press, pp. 12–133.

774 Blanchard, D. C., & Blanchard, R. J (1990b). Anti-predator defence as models of animal fear and
775 anxiety. In P. F. Brain, S. Parmigiani, R. J. Blanchard, & D. Blanchard (Eds.), *Fear and*
776 *defence* (pp. 89-105). Chur, Switzerland: Harwood Academic.

777 Blanchard, R. J., Griebel, G., Henrie, J. A., & Blanchard, D. C. (1997). Differentiation of
778 anxiolytic and panicolytic drugs by effects on rat and mouse defense test
779 batteries. *Neuroscience & Biobehavioral Reviews*, *21*(6), 783-789.

Blanchard, D. C., Griebel, G., & Blanchard, R. J. (2001). Mouse defensive behaviors: pharmacological and behavioral assays for anxiety and panic. *Neuroscience & Biobehavioral Reviews*, *25*(3), 205-218.

Bossola, M., Angioletti, L., Di Stasio, E., Vulpio, C., De Filippis, D., & Balconi, M. (2020). Reward (BIS/BAS) mechanisms and fatigue in patients on chronic hemodialysis. *Psychology, health & medicine*, *25*(6), 710-718.

Botvinick, M. M., Cohen, J. D., & Carter, C. S. (2004). Conflict monitoring and anterior cingulate cortex: an update. *Trends in cognitive sciences*, *8*(12), 539-546.

Breiter, H. C., Aharon, I., Kahneman, D., Dale, A., & Shizgal, P. (2001). Functional imaging of neural responses to expectancy and experience of monetary gains and losses. *Neuron*, *30*(2), 619-639.

Bunford, N., Roberts, J., Kennedy, A. E., & Klumpp, H. (2017). Neurofunctional correlates of behavioral inhibition system sensitivity during attentional control are modulated by perceptual load. *Biological Psychology*, *127*, 10-17.

Carver, C. S., & White, T. L. (1994). Behavioral inhibition, behavioral activation, and affective responses to impending reward and punishment: the BIS/BAS scales. *Journal of personality and social psychology*, *67*(2), 319.

Cherbuin, N., Windsor, T. D., Anstey, K. J., Maller, J. J., Meslin, C., & Sachdev, P. S. (2008). Hippocampal volume is positively associated with behavioural inhibition (BIS) in a large community-based sample of mid-life adults: the PATH through life study. *Social cognitive and affective neuroscience*, *3*(3), 262-269.

Corr, P. J. (2002). JA Gray's reinforcement sensitivity theory: Tests of the joint subsystems hypothesis of anxiety and impulsivity. *Personality and individual differences*, *33*(4), 511-532.

Corr, P. J. (2016). Reinforcement sensitivity theory of personality questionnaires: Structural survey with recommendations. *Personality and Individual Differences*, 89, 60-64.

Corr, P. J., & Cooper, A. J. (2016). The Reinforcement Sensitivity Theory of Personality Questionnaire (RST-PQ): Development and validation. *Psychological assessment*, *28*(11), 1427.

Costumero, V., Barrós-Loscertales, A., Bustamante, J. C., Ventura-Campos, N., Fuentes, P., Rosell-Negre, P., & Ávila, C. (2013b). Reward sensitivity is associated with brain activity during erotic stimulus processing. *PLoS One*, *8*(6), e66940.

Costumero, V., Barrós- Loscertales, A., Bustamante, J. C., Ventura- Campos, N., Fuentes, P., & Ávila, C. (2013a). Reward sensitivity modulates connectivity among reward brain areas during processing of anticipatory reward cues. *European Journal of Neuroscience*, *38*(3), 2399-2407.

Costumero, V., Barrós-Loscertales, A., Fuentes, P., Rosell-Negre, P., Bustamante, J. C., & Ávila, C. (2016). BAS-drive trait modulates dorsomedial striatum activity during reward response-outcome associations. *Brain imaging and behavior*, *10*(3), 869-879.

Costumero, V., Barrós-Loscertales, A., Bustamante, J. C., Fuentes, P., Rosell-Negre, P., Ventura-Campos, N., & Avila, C. (2015). A new window to understanding individual differences in reward sensitivity from attentional networks. *Brain Structure and Function*, *220*(3), 1807-1821.

Davidow, J. Y., Foerde, K., Galván, A., & Shohamy, D. (2016). An upside to reward sensitivity: the hippocampus supports enhanced reinforcement learning in adolescence. *Neuron*, *92*(1), 93-99.

Davis, M. (1992). The role of the amygdala in fear and anxiety. *Annual review of neuroscience*, *15*(1), 353-375.

Davis, M., Walker, D. L., Miles, L., & Grillon, C. (2010). Phasic vs sustained fear in rats and humans: role of the extended amygdala in fear vs anxiety. *Neuropsychopharmacology*, *35*(1), 105-135.

Deng, H., Xiao, X., & Wang, Z. (2016). Periaqueductal gray neuronal activities underlie different aspects of defensive behaviors. *Journal of Neuroscience*, *36*(29), 7580-7588.

Dong, G., Li, H., Wang, Y., & Potenza, M. N. (2018). Individual differences in self-reported reward-approach tendencies relate to resting-state and reward-task-based fMRI measures. *International Journal of Psychophysiology*, *128*, 31-39.

Downes, M. J., Brennan, M. L., Williams, H. C., & Dean, R. S. (2016). Development of a critical appraisal tool to assess the quality of cross-sectional studies (AXIS). *BMJ open*, *6*(12), e011458.

Eichenbaum, H. (2017). The role of the hippocampus in navigation is memory. *Journal of neurophysiology*, *117*(4), 1785-1796.

Einarsson, E. Ö., & Nader, K. (2012). Involvement of the anterior cingulate cortex in formation, consolidation, and reconsolidation of recent and remote contextual fear memory. *Learning & memory*, *19*(10), 449-452.

Eryilmaz, H., Rodriguez-Thompson, A., Tanner, A. S., Giegold, M., Huntington, F. C., & Roffman, J. L. (2017). Neural determinants of human goal-directed vs. habitual action control and their relation to trait motivation. *Scientific reports*, *7*(1), 1-11.

Fiddick, L. (2011). There is more than the amygdala: potential threat assessment in the cingulate cortex. *Neuroscience & Biobehavioral Reviews*, *35*(4), 1007-1018.

Fineberg, N. A., Apergis-Schoute, A. M., Vaghi, M. M., Banca, P., Gillan, C. M., Voon, V., ... & Bullmore, E. T. (2018). Mapping compulsivity in the DSM-5 obsessive compulsive and related disorders: cognitive domains, neural circuitry, and treatment. *International Journal of Neuropsychopharmacology*, *21*(1), 42-58.

Fox, A. S., & Shackman, A. J. (2019). The central extended amygdala in fear and anxiety: Closing the gap between mechanistic and neuroimaging research. *Neuroscience letters*, *693*, 58-67.

Fuentes-Claramonte, P., Ávila, C., Rodríguez-Pujadas, A., Costumero, V., Ventura-Campos, N., Bustamante, J. C., ... & Barrós-Loscertales, A. (2016). Characterizing individual differences in reward sensitivity from the brain networks involved in response inhibition. *Neuroimage*, *124*, 287-299.

Fuentes-Claramonte, P., Ávila, C., Rodríguez-Pujadas, A., Costumero, V., Ventura-Campos, N., Bustamante, J. C., ... & Barrós-Loscertales, A. (2016). Inferior frontal cortex activity is modulated by reward sensitivity and performance variability. *Biological Psychology*, *114*, 127-137.

Fuentes-Claramonte, P., Ávila, C., Rodríguez-Pujadas, A., Ventura-Campos, N., Bustamante, J. C., Costumero, V., ... & Barrós-Loscertales, A. (2015). Reward sensitivity modulates

brain activity in the prefrontal cortex, ACC and striatum during task switching. *PLoS One, 10*(4), e0123073.

Furl, N., & Averbeck, B. B. (2011). Parietal cortex and insula relate to evidence seeking relevant to reward-related decisions. *Journal of Neuroscience, 31*(48), 17572-17582.

Frankland, P. W., Bontempi, B., Talton, L. E., Kaczmarek, L., & Silva, A. J. (2004). The involvement of the anterior cingulate cortex in remote contextual fear memory. *Science, 304*(5672), 881-883.

Gray, J. A. (1982). Précis of The neuropsychology of anxiety: An enquiry into the functions of the septo-hippocampal system. *Behavioral and Brain Sciences, 5*(3), 469-484.

Gray, J. R., & Braver, T. S. (2002). Personality predicts working-memory—related activation in the caudal anterior cingulate cortex. *Cognitive, Affective, & Behavioral Neuroscience, 2(1),* 64-75.

Gray, J. R., Burgess, G. C., Schaefer, A., Yarkoni, T., Larsen, R. J., & Braver, T. S. (2005). Affective personality differences in neural processing efficiency confirmed using fMRI. *Cognitive, Affective, & Behavioral Neuroscience, 5*(2), 182-190.

Glover, G. H. (2011). Overview of functional magnetic resonance imaging. Neurosurgery Clinics, 22(2), 133-139.

Griebel, G., Blanchard, D. C., Jung, A., Masuda, C. K., & Blanchard, R. J. (1995). 5-HT1A agonists modulate mouse antipredator defensive behavior differently from the 5-HT2A antagonist pirenperone. *Pharmacology Biochemistry and Behavior, 51*(2-3), 235-244.

886 Gross, C. T., & Canteras, N. S. (2012). The many paths to fear. *Nature Reviews Neuroscience*,
887 *13*(9), 651-658.

888 Gui, X. U. E., Chuansheng, C. H. E. N., Zhong-Lin, L. U., & Qi, D. O. N. G. (2010). Brain
889 imaging techniques and their applications in decision-making research. Xin li xue bao.
890 Acta psychologica Sinica, 42(1), 120.

891 Haber, S. N. (2011). Neuroanatomy of Reward: A View from the Ventral Striatum.
892 *Neurobiology of sensation and reward*, 235.

893 Haber, S. N., & Knutson, B. (2010). The reward circuit: linking primate anatomy and human
894 imaging. *Neuropsychopharmacology*, *35*(1), 4-26.

895 Hahn, T., Dresler, T., Ehlis, A. C., Pyka, M., Dieler, A. C., Saathoff, C., ... & Fallgatter, A. J.
896 (2012). Randomness of resting-state brain oscillations encodes Gray's personality
897 trait. *Neuroimage*, *59*(2), 1842-1845.

898 Hahn, T., Dresler, T., Ehlis, A. C., Plichta, M. M., Heinzel, S., Polak, T., ... & Fallgatter, A. J.
899 (2009). Neural response to reward anticipation is modulated by Gray's
900 impulsivity. *Neuroimage*, *46*(4), 1148-1153.

901 Hahn, T., Dresler, T., Plichta, M. M., Ehlis, A. C., Ernst, L. H., Markulin, F., ... & Fallgatter, A.
902 J. (2010). Functional amygdala-hippocampus connectivity during anticipation of aversive
903 events is associated with Gray's trait "sensitivity to punishment". *Biological*
904 *psychiatry*, *68*(5), 459-464.

905 Hahn, T., Dresler, T., Pyka, M., Notebaert, K., & Fallgatter, A. J. (2013). Local synchronization
906 of resting-state dynamics encodes gray's trait anxiety. *PLoS One*, *8*(3), e58336.

Hahn, T., Heinzel, S., Dresler, T., Plichta, M. M., Renner, T. J., Markulin, F., ... & Fallgatter, A. J. (2011). Association between reward- related activation in the ventral striatum and trait reward sensitivity is moderated by dopamine transporter genotype. *Human brain mapping*, *32*(10), 1557-1565.

Hahn, T., Heinzel, S., Notebaert, K., Dresler, T., Reif, A., Lesch, K. P., ... & Fallgatter, A. J. (2013). The tricks of the trait: neural implementation of personality varies with genotype-dependent serotonin levels. *Neuroimage*, *81*, 393-399.

Harmon-Jones, E. (2003). Anger and the behavioral approach system. *Personality and Individual differences*, 35(5), 995-1005.

Heimer, L., De Olmos, J. S., Alheid, G. F., Pearson, J., Sakamoto, N., Shinoda, K., ... & Switzer, R. C. (1999). The human basal forebrain. Part II. *Handbook of chemical neuroanatomy*, 15, 57-226.

Heym, N., Ferguson, E., & Lawrence, C. (2008). An evaluation of the relationship between Gray's revised RST and Eysenck's PEN: Distinguishing BIS and FFFS in Carver and White's BIS/BAS scales. *Personality and Individual Differences*, *45*(8), 709-715.

Jackson, C. J. (2009). Jackson-5 scales of revised Reinforcement Sensitivity Theory (r-RST) and their application to dysfunctional real world outcomes. *Journal of Research in Personality*, *43*(4), 556-569.

Jeena, R. S., & Kumar, S. (2013). A comparative analysis of MRI and CT brain images for stroke diagnosis. In 2013 Annual International Conference on Emerging Research Areas and 2013 International Conference on Microelectronics, Communications and Renewable Energy (pp. 1-5). IEEE.

Keifer Jr, O. P., Hurt, R. C., Ressler, K. J., & Marvar, P. J. (2015). The physiology of fear: reconceptualizing the role of the central amygdala in fear learning. *Physiology*, *30*(5), 389-401.

Knutson, B., Adams, C. M., Fong, G. W., & Hommer, D. (2001). Anticipation of increasing monetary reward selectively recruits nucleus accumbens. *Journal of Neuroscience*, *21*(16), RC159-RC159.

Knutson, B., & Bossaerts, P. (2007). Neural antecedents of financial decisions. *Journal of Neuroscience*, *27*(31), 8174-8177.

Kühn, S., & Gallinat, J. (2011). A quantitative meta- analysis on cue- induced male sexual arousal. *The journal of sexual medicine*, *8*(8), 2269-2275.

Kumari, V., Antonova, E., Geyer, M. A., Ffytche, D., Williams, S. C., & Sharma, T. (2007). A fMRI investigation of startle gating deficits in schizophrenia patients treated with typical or atypical antipsychotics. *International Journal of Neuropsychopharmacology*, *10*(4), 463-477.

Krupić, D., & Corr, P. J. (2017). Moving forward with the BAS: Towards a neurobiology of multidimensional model of approach motivation. *Psychological Topics*, *26*(1), 25-45.

Krupić, D., Corr, P. J., Ručević, S., Križanić, V., & Gračanin, A. (2016). Five reinforcement sensitivity theory (RST) of personality questionnaires: Comparison, validity and generalization. *Personality and Individual Differences*, *97*, 19-24.

948 Lansink, C. S., Goltstein, P. M., Lankelma, J. V., McNaughton, B. L., & Pennartz, C. M. (2009).
949 Hippocampus leads ventral striatum in replay of place-reward information. *PLoS Biol*,
950 *7*(8), e1000173.

951 LeDoux, J. E. (1994). Emotion, memory and the brain. *Scientific American*, *270*(6), 50-57.

952 Leech, R., & Sharp, D. J. (2014). The role of the posterior cingulate cortex in cognition and
953 disease. *Brain*, *137*(1), 12-32.

954 Levita, L., Bois, C., Healey, A., Smyllie, E., Papakonstantinou, E., Hartley, T., & Lever, C.
955 (2014). The Behavioural Inhibition System, anxiety and hippocampal volume in a non-
956 clinical population. *Biology of mood & anxiety disorders*, *4*(1), 1-10.

957 Li, Y., Qiao, L., Sun, J., Wei, D., Li, W., Qiu, J., ... & Shi, H. (2014). Gender-specific
958 neuroanatomical basis of behavioral inhibition/approach systems (BIS/BAS) in a large
959 sample of young adults: a voxel-based morphometric investigation. *Behavioural brain*
960 *research*, *274*, 400-408.

961 Liu, X., Hairston, J., Schrier, M., & Fan, J. (2011). Common and distinct networks underlying
962 reward valence and processing stages: a meta-analysis of functional neuroimaging
963 studies. *Neuroscience & Biobehavioral Reviews*, *35*(5), 1219-1236.

964 Luking, K. R., & Barch, D. M. (2013). Candy and the brain: neural response to candy gains and
965 losses. *Cognitive, Affective, & Behavioral Neuroscience*, *13*(3), 437-451.

966 McNaughton, N. (1997). Cognitive dysfunction resulting from hippocampal hyperactivity—a
967 possible cause of anxiety disorder?. *Pharmacology Biochemistry and Behavior*, *56*(4),
968 603-611.

McNaughton, N., & Gray, J. A. (2000). Anxiolytic action on the behavioural inhibition system implies multiple types of arousal contribute to anxiety. *Journal of affective disorders*, *61*(3), 161-176.

Milad, M. R., Quirk, G. J., Pitman, R. K., Orr, S. P., Fischl, B., & Rauch, S. L. (2007). A role for the human dorsal anterior cingulate cortex in fear expression. *Biological psychiatry*, *62*(10), 1191-1194.

Milne, E., & Grafman, J. (2001). Ventromedial prefrontal cortex lesions in humans eliminate implicit gender stereotyping. *Journal of Neuroscience*, *21*(12), RC150-RC150.

Moher, D., Liberati, A., Tetzlaff, J., Altman, D. G., & Prisma Group. (2009). Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. *PLoS medicine, 6(7)*, e1000097.

Mortensen, J. A., Lehn, H., Evensmoen, H. R., & Håberg, A. K. (2015). Evidence for an antagonistic interaction between reward and punishment sensitivity on striatal activity: A verification of the Joint Subsystems Hypothesis. *Personality and Individual Differences*, *74*, 214-219.

Motta, S. C., Carobrez, A. P., & Canteras, N. S. (2017). The periaqueductal gray and primal emotional processing critical to influence complex defensive responses, fear learning and reward seeking. *Neuroscience & Biobehavioral Reviews*, *76*, 39-47.

Motta, S. C., Goto, M., Gouveia, F. V., Baldo, M. V., Canteras, N. S., & Swanson, L. W. (2009). Dissecting the brain's fear system reveals the hypothalamus is critical for responding in subordinate conspecific intruders. *Proceedings of the National Academy of Sciences*, *106*(12), 4870-4875.

Murray, E. A. (2007). The amygdala, reward and emotion. *Trends in cognitive sciences*, *11*(11), 489-497.

Neseliler, S., Tannenbaum, B., Zacchia, M., Larcher, K., Coulter, K., Lamarche, M., ... & Dagher, A. (2017). Academic stress and personality interact to increase the neural response to high-calorie food cues. *Appetite*, *116*, 306-314.

O'Doherty, J., Kringelbach, M. L., Rolls, E. T., Hornak, J., & Andrews, C. (2001). Abstract reward and punishment representations in the human orbitofrontal cortex. *Nature neuroscience*, *4*(1), 95-102.

O'Doherty, J. P., Buchanan, T. W., Seymour, B., & Dolan, R. J. (2006). Predictive neural coding of reward preference involves dissociable responses in human ventral midbrain and ventral striatum. *Neuron*, *49*(1), 157-166.

Ogawa, S., Lee, T. M., Stepnoski, R., Chen, W., Zhu, X. H., & Ugurbil, K. (2000). An approach to probe some neural systems interaction by functional MRI at neural time scale down to milliseconds. *Proceedings of the National Academy of Sciences*, *97(20)*, 11026-11031.

Oldham, S., Murawski, C., Fornito, A., Youssef, G., Yücel, M., & Lorenzetti, V. (2018). The anticipation and outcome phases of reward and loss processing: A neuroimaging meta-analysis of the monetary incentive delay task. *Human brain mapping*, *39*(8), 3398-3418.

Pascucci, D., Hickey, C., Jovicich, J., & Turatto, M. (2017). Independent circuits in basal ganglia and cortex for the processing of reward and precision feedback. *Neuroimage*, *162*, 56-64.

Peters, J., & Büchel, C. (2010). Neural representations of subjective reward value. *Behavioural brain research*, *213*(2), 135-141.

1012 Pickering, A. D. (2008). Formal and computational models of Reinforcement Sensitivity Theory.
1013 *The reinforcement sensitivity theory of personality*, 453.

1014 Pickering, A. D., & Corr, P. J. (2008). JA Gray's reinforcement sensitivity theory (RST) of
1015 personality. *The SAGE handbook of personality: Theory and assessment personality*
1016 *measurement and testing*, *2*, 239-255.

1017 Pickering, A. D., Corr, P. J., & Gray, J. A. (1999). Interactions and reinforcement sensitivity
1018 theory: A theoretical analysis of Rusting and Larsen (1997).

1019 Pickering, A. D., & Smillie, L. D. (2008). The behavioural activation system: Challenges and
1020 opportunities. *The reinforcement sensitivity theory of personality*, 120-154.

1021 Qiu, C., Liao, W., Ding, J., Feng, Y., Zhu, C., Nie, X., ... & Gong, Q. (2011). Regional
1022 homogeneity changes in social anxiety disorder: a resting-state fMRI study. *Psychiatry*
1023 *Research: Neuroimaging*, *194*(1), 47-53.

1024 Quadflieg, S., Turk, D. J., Waiter, G. D., Mitchell, J. P., Jenkins, A. C., & Macrae, C. N. (2009).
1025 Exploring the neural correlates of social stereotyping. *Journal of Cognitive Neuroscience*,
1026 *21*(8), 1560-1570.

1027 Radke, S., Seidel, E. M., Eickhoff, S. B., Gur, R. C., Schneider, F., Habel, U., & Derntl, B.
1028 (2016). When opportunity meets motivation: neural engagement during social approach
1029 is linked to high approach motivation. *NeuroImage*, *127*, 267-276.

1030 Reuter, M., Cooper, A. J., Smillie, L. D., Markett, S., & Montag, C. (2015). A new measure for
1031 the revised reinforcement sensitivity theory: Psychometric criteria and genetic validation.
1032 *Frontiers in systems neuroscience*, 9, 38.

Reuter, M., Stark, R., Hennig, J., Walter, B., Kirsch, P., Schienle, A., & Vaitl, D. (2004). Personality and emotion: test of Gray's personality theory by means of an fMRI study. *Behavioral Neuroscience*, *118*(3), 462.

Roy, M., Shohamy, D., Daw, N., Jepma, M., Wimmer, G. E., & Wager, T. D. (2014). Representation of aversive prediction errors in the human periaqueductal gray. *Nature neuroscience*, *17*(11), 1607-1612.

Rushworth, M. F., Noonan, M. P., Boorman, E. D., Walton, M. E., & Behrens, T. E. (2011). Frontal cortex and reward-guided learning and decision-making. *Neuron*, *70*(6), 1054-1069.

Sescousse, G., Caldú, X., Segura, B., & Dreher, J.-C. C. (2013). Processing of primary and secondary rewards: a quantitative meta-analysis and review of human functional neuroimaging studies. Neuroscience and Biobehavioral Reviews, 37(4), 681–696.

Simon, J. J., Walther, S., Fiebach, C. J., Friederich, H. C., Stippich, C., Weisbrod, M., & Kaiser, S. (2010). Neural reward processing is modulated by approach-and avoidance-related personality traits. *Neuroimage*, *49*(2), 1868-1874.

Smederevac, S., Mitrović, D., Čolović, P., & Nikolašević, Ž. (2014). Validation of the measure of revised reinforcement sensitivity theory constructs. *Journal of Individual Differences*.

Smillie, L. D. (2008). What is reinforcement sensitivity? Neuroscience paradigms for approach-avoidance process theories of personality. *European Journal of Personality*, 22(5), 359-384.

Smillie, L. D., Pickering, A. D., & Jackson, C. J. (2006). The new reinforcement sensitivity theory: Implications for personality measurement. *Personality and Social Psychology Review*, *10*(4), 320-335.

Smith, K. S., Tindell, A. J., Aldridge, J. W., & Berridge, K. C. (2009). Ventral pallidum roles in reward and motivation. *Behavioural brain research*, *196*(2), 155-167.

Staudinger, M. R., Erk, S., & Walter, H. (2011). Dorsolateral prefrontal cortex modulates striatal reward encoding during reappraisal of reward anticipation. *Cerebral cortex*, *21*(11), 2578-2588.

Strauman, T. J., Detloff, A. M., Sestokas, R., Smith, D. V., Goetz, E. L., Rivera, C., & Kwapil, L. (2013). What shall I be, what must I be: neural correlates of personal goal activation. *Frontiers in integrative neuroscience*, *6*, 123.

Sun, J., Luo, Y., Chang, H., Zhang, R., Liu, R., Jiang, Y., & Xi, H. (2020). The Mediating Role of Cognitive Emotion Regulation in BIS/BAS Sensitivities, Depression, and Anxiety Among Community-Dwelling Older Adults in China. *Psychology Research and Behavior Management*, *13*, 939.

Tang, J., Ko, S., Ding, H. K., Qiu, C. S., Calejesan, A. A., & Zhuo, M. (2005). Pavlovian fear memory induced by activation in the anterior cingulate cortex. *Molecular pain*, *1*, 1744-8069.

Teyler, T. J., & DiScenna, P. (1985). The role of hippocampus in memory: a hypothesis. *Neuroscience & Biobehavioral Reviews*, *9*(3), 377-389.

Torrubia, R., Avila, C., Moltó, J., & Caseras, X. (2001). The Sensitivity to Punishment and Sensitivity to Reward Questionnaire (SPSRQ) as a measure of Gray's anxiety and impulsivity dimensions. *Personality and individual differences*, *31*(6), 837-862.

Trutti, A. C., Mulder, M. J., Hommel, B., & Forstmann, B. U. (2019). Functional neuroanatomical review of the ventral tegmental area. *NeuroImage*, *191*, 258-268.

Tull, M. T., Gratz, K. L., Latzman, R. D., Kimbrel, N. A., & Lejuez, C. W. (2010). Reinforcement sensitivity theory and emotion regulation difficulties: A multimodal investigation. *Personality and Individual Differences*, *49*(8), 989-994.

van Rijn, I., Griffioen-Roose, S., de Graaf, C., & Smeets, P. A. (2016). Neural processing of calories in brain reward areas can be modulated by reward sensitivity. *Frontiers in behavioral neuroscience*, *9*, 371.

Walker, B. R., & Jackson, C. J. (2017). Examining the validity of the revised Reinforcement Sensitivity Theory scales. *Personality and Individual Differences*, *106*, 90-94.

Wallace, L., Heym, N., Sumich, A., & Fido, D. (2020). A systematic review on the current conceptualisations of successful psychopathy. https://doi.org/10.31234/osf.io/wkjrm

Wallis, J. D., & Kennerley, S. W. (2010). Heterogeneous reward signals in prefrontal cortex. *Current opinion in neurobiology*, *20*(2), 191-198.

Wheelock, M. D., Sreenivasan, K. R., Wood, K. H., Ver Hoef, L. W., Deshpande, G., & Knight, D. C. (2014). Threat-related learning relies on distinct dorsal prefrontal cortex network connectivity. *Neuroimage*, *102*, 904-912.

Wright, P., He, G., Shapira, N. A., Goodman, W. K., & Liu, Y. (2004). Disgust and the insula: fMRI responses to pictures of mutilation and contamination. *Neuroreport*, *15*(15), 2347-2351.

Xu, J., Kober, H., Carroll, K. M., Rounsaville, B. J., Pearlson, G. D., & Potenza, M. N. (2012). White matter integrity and behavioral activation in healthy subjects. *Human brain mapping*, *33*(4), 994-1002.

Zhao, X. H., Wang, P. J., Li, C. B., Hu, Z. H., Xi, Q., Wu, W. Y., & Tang, X. W. (2007). Altered default mode network activity in patient with anxiety disorders: an fMRI study. *European journal of radiology*, *63*(3), 373-378.

Table 1

Authors	N	Age Mean (SD)	Sex Men %	RST scale	Tasks	Relevant findings	Acquisition method	Scanner
Adrian-Ventura et al., 2019a	89	22.4 (4.7)	35	SRSPQ (only SR)	Resting state connectivity	Positive correlation between SR and connectivity between the ACC and vmPFC and the vmPFC and VTA	T2* EPI	1.5T Siemens Avanto
Adrian-Ventura et al., 2019b	400	23.1 (5.3)	58	SRSPQ	GMV	Negative correlation between SR and GMV in the ACC, medial PFC, left lateral PFC, left middle and superior temporal lobe and left insula for both genders. Negative correlation between SR and GMV in the left NAcc and caudate for males. Positive correlation between SP and GMV of the left amygdala in males.	T1* MPRAGE	1.5T Siemens Avanto
Angelides et al., 2017	47	22 (3.8)	45	BIS/BAS	Resting state connectivity	Positive correlation between BAS fun-seeking and connectivity between the OFC and putamen. Negative correlation between BAS Drive and connectivity between the medial cingulate cortex and the caudate	T2* Multi-band EPI	3T Siemens Trio
Avila et al., 2012	31	25 (5.9)	100	SRSPQ (only SR)	Set switching	Positive correlation between SR and activity in the right VS and right IFG. Negative correlation between SR and activity in the rostral ACC.	T2* EPI	1.5T Siemens Avanto
Barros-Loscertales et al., 2006a	63	22.43 (-)	100	SRSPQ (only SP)	GMV	Positive correlation between SP and GMV of right parahippocampus, hippocampus and amygdala and the left anterior parahippocampus.	T1* FFE	1.5T Siemens Sonata
Barros-Loscertales et al., 2006b	50	22.43 (-)	100	SRSPQ (Only SR)	GMV	Negative correlation between SR and GMV right caudate, putamen and superior frontal cortex as well as the left caudate, putamen and globus pallidus	T1* FFE	1.5T Siemens Sonata
Barros-Loscertales et al., 2010	45	21.8 (-)	100	SRSPQ (only SR)	Affective pictures (aversive & erotic)	Erotic pictures: positive correlation between SR and activity in the medial PFC, left lateral PFC, right occipital gyrus and precuneus and a negative correlation in the superior frontal gyrus. Aversive images: negative correlation between SR and activity in the left occipital cortex and right lateral PFC.	T2* EPI	1.5T Siemens Avanto
Beaver et al., 2006	12	22 (2.4)	42	BIS/BAS (only BAS)	Food cues	Positive correlation between BAS-Drive and activity in the left OFC, right VS, left Amygdala, the VTA/substantia nigra and left VPal and between BAS	T2* EPI	3T Medspec

						reward responsiveness and activity in the OFC and VPal when comparing appetizing to bland foods. Positive correlation between BAS-drive and activity in the right OFC and right VS when viewing disgusting food images compared to bland.		
Bunford et al., 2017	30	25.6 (7.0)		BIS/BAS (only BIS)	Affective pictures (angry & fearful faces)	Angry: Greater activation of the left dlPFC seen in high BIS condition. Fearful: Greater activation of the right dorsal ACC in high BIS condition.	T2* Spiral	3T GE Signa
Cherbun et al., 2008	430	M: 46.6 (1.5) F: 46.7 (1.4)	46	BIS/BAS	GMV	Positive correlation between BIS and GMV in the hippocampus.	T1* FFE	1.5 Tesla Gyroscan
Costumero et al., 2013a	44	23.4 (4.1)	100	SRSPQ (only SR)	MID task	Positive correlation between SR and activity in the right NAcc and left midbrain when processing reward cues. Negative correlations between SR and connectivity between the midbrain and the medial OFC during incentive processing and between SR and connectivity between the NAcc and left amygdala during reward anticipation.	T2* EPI	1.5T Siemens Avanto
Costumero et al., 2015	Exp 1: 41 Exp 2: 30	Exp 1: 23.3 (4.2) Exp 2: 23.7 (3.0)	100	SRSPQ (only SR)	Monetary incentive delay task (MID; experiment 1) Affective pictures (erotic; experiment 2)	Experiment 1: Positive correlation between SR and activity in the DMN and right frontoparietal network (FPN) during anticipation of rewards and punishments. Experiment 2: SR scores correlated negatively with DMN modulation at onset of full and partial reward cues. Positive correlation between SR and FPN modulation during full and partial reward cues.	T2* EPI	1.5T Siemens Avanto
Costumero et al., 2016	45	26.4 (5.4)	100	BIS/BAS (Only BAS)	Gambling task (rewards and punishments)	Positive correlation between BAS-Drive and activity in the left dorsomedial striatum and left VS on receipt of reward.	T2* EPI	1.5T Siemens Avanto

Customero et al., 2013b	45	24.08 (3.71)	100	SRSPQ (only SR)	Affective Pictures (erotic)	Positive correlation between SR and activity in the left OFC, left insula and left VS when viewing erotic images.	T2* EPI	1.5T Siemens Avanto
Dingra et al., 2021	63	37 (11)	57	SRSPQ	MID task	Positive correlation between SR and activity in the PCC and precuneus when comparing dollar wins to nil for males only. Negative correlation between SP and activity in the right middle frontal and postcentral gyri when comparing dollar wins to nil for women only. A negative correlation between SP and activity in the right anterior insula, left superior frontal gyrus and right temporal gyrus when comparing dollar to cent wins for women only.	EPI	3T Siemens
Dong et al., 2018	191	21.3 (1.3)	53	BIS/BAS (Only BAS)	Resting state connectivity Money incentive card guessing task	Resting state: Positive correlation between BAS and connectivity between the left and right striatum and the right frontal gyrus and right striatum. Task: Positive correlation between BAS and activity in the right striatum when receiving reward.	Resting: T1* FSPGR, Task: T2* EPI	3T Siemens Trio
Eryilmaz et al., 2017	72	24.7 (-)	49	BIS/BAS	Monetary reward (discriminatio n learning task, outcome devaluation task, slip task)	No correlations survived false discovery rate corrections.	T2* EPI	3T Siemens Skyra
Fuentas-Claramonte et al., 2016	57	21.5 (2.4)	58	SRSPQ (only SR)	Go/No Go task	Positive correlation between SR and activity in the IFG for no-go and infrequent go.	T2* EPI	1.5T Siemens Avanto
Funetas-Claramonet et al., 2015	28	24.2 (4.1)	46	SRSPQ (only SR)	Set switching	Positive correlation between SR and activity in the IFG, dlPFC, ACC, inferior parietal cortex and post central gyrus when comparing switch to repeat cues. Negative correlation between SR and activity in the VS while processing switch cues.	T2* EPI	1.5T Siemens Avanto
Funetas-Claramonet et al., 2016	50	21.6 (2.6)	60	SRSPQ (only SR)	Go/No Go task	Positive correlation between SR and activity in the pre and post central gyri, superior parietal cortex, supplementary motor area and right cerebellum during stop errors. Negative correlation between SR and activity in the left FPN and anterior DMN during	T2* EPI	1.5T Siemens Avanto

						stop errors. Negative correlation between SR and activity in the midline network (includes ACC, SMA and insula) during stop signal trials.		
Gray & Braver, 2002	14	-(-; range between 19-27)	43	BIS/BAS	N-back task after watching affective videos (pleasant, neutral, unpleasant)	Negative correlation between BAS and activity in the caudal and posterior rostral ACC for all conditions. Positive correlation between BIS and activity in the caudal ACC for pleasant stimuli.	T2* Spin Echo EPI	1.5T Siemens Vision
Gray et al., 2005	60	-(-; range between 18-37)	48	BIS/BAS	N-back task	Negative correlation between BAS and item-related activity in the dorsal ACC, PFC and parietal cortex. Positive correlation between BIS and state-related activity in the rostral ACC. Positive correlation between BAS and state-related activity in the parietal cortex.	T2* EPI	1.5T Siemens
Hahn et al ., 2013	89	27.8 (7.5)	45	SRSPQ	MID task (only loss)	Positive correlation between SP and connectivity between the amygdala and hippocampus during loss anticipation. No correlations with activity.	T2* EPI	1.5T Siemens Magnetom Avanto
Hahn et al., 2009	20	29.4 (7.6)	40	SRSPQ	MID task (only gains)	Positive correlation between SR and activity in the right VS and right OFC during large reward trials	T2* EPI	1.5T Siemens Magnetom Avanto
Hahn et al., 2010	45	291. (7.7)	42	SRSPQ	MID task (only loss)	Positive correlation between SP and activity in right amygdala and right hippocampus during high loss anticipation. No correlations with activity in amygdala and hippocampus.	T2* EPI	1.5T Siemens Magnetom Avanto
Hahn et al., 2011	53	29 (7.6)	40*	SRSPQ	MID task (only gains)	Positive correlation between SR and activity in the VS during reward anticipation.	T2* EPI	1.5T Siemens Magnetom Avanto
Hahn et al., 2012	15	24.4 (3.2)	100	SRSPQ	Hurst component	Positive correlation between SR and the Hurst component in the ventral striatum and OFC.	T2* EPI	1.5T Siemens Magnetom Avanto

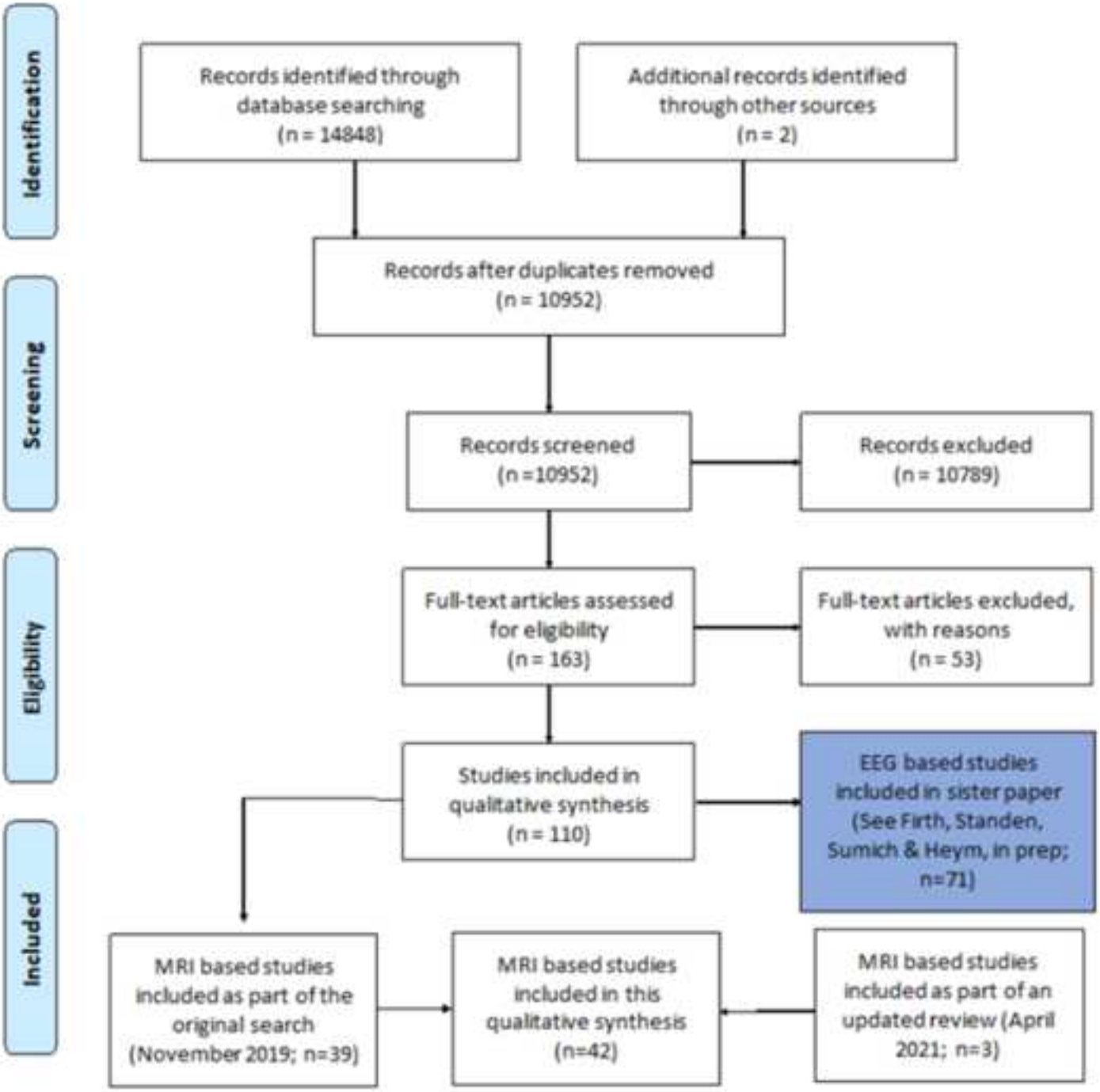
Hahn et al., 2013	27	25.5 (3.38)	52	SRSPQ	Regional Homogeneity	Negative correlation between SP and regional homogeneity in the amygdala and hippocampus.	T2* EPI	1.5T Siemens Magnetom Avanto
Levita et al., 2014	30	24.1 (2.66)	54	SRSPQ (only SP)	GMV	Positive correlation between SP and GMV of the right hippocampus.	T1* FSPGR	3T GE Excite
Li et al., 2014	350	M: 20.1 (1.4) F: 19.8 (1.2)	45	BIS/BAS	GMV	Females displayed a negative correlation between BIS and GMV in the parrahippocampus and positive correlations between BAS and GMV in the vmPFC and inferior parietal lobe. This pattern was the opposite in males.	T1* MPRAGE	3T Siemens Magnetom
Luking et al., 2013	20	24 (1.4)	40	BIS/BAS	Card guessing (sweets as reward)	Positive correlation between BAS and activity in the IFG for low loss trials. Positive correlation between BAS and activity in the right caudate and right OFC when comparing low loss to neutral. Negative correlation between BAS and activity in right caudate and right OFC when comparing high to low loss trials.	T2* EPI	3T Siemens Trio
Mortensen et al., 2015	15	27 (-; range between 19-41)	0	SRSPQ (and neuroticism)	Priming task	Positive correlation between SR scores and activity in left caudate, left NAcc, left posterior hippocampus, right medial OFC and left thalamus in various contrasts. Joint sub-system scores (SR+/-SP & SR+/N) correlated with the same areas were better predictors of activity in the left caudate and NAcc.	T2* EPI	3T Phillips Intera
Neseliler et al., 2017	22	20.5 (2.9)	41	BIS/BAS	Food and scenery images	Negative correlation between BIS and connectivity between the vmPFC and dlPFC when looking at high compared to low calorie food during exam time period. Positive correlation between BIS and activity in vmPFC and amygdala in response to high calorie food.	T2* EPI	3T Siemens Magnetom
Parcet et al., 2020	206	23.7 (6.7)	52	SRSPQ	GMW	A negative correlation between SR and GMV in the left caudate.	T1* MPRAGE	1.5T Siemens Avanto
Park et al., 2021	31	22.7 (3.3)	42	BIS/BAS SRSPQ	White Matter	A negative correlation between BIS and the number of white matter fibres in corpus callosum , the fibre density in the unicate fasciculus and the number of fibres in the right and left accumbofrontal tracts.	Diffusion weighted MRI	3T Siemens Magnetom Trio

Pascucci et al., 2017	20	24 (3)	30	BIS/BAS	Monetary reward: shooting task	Positive correlation between BAS and activity in the NAcc during precision feedback.	T2* EPI	4T Medspec Biospin
Radke et al., 2016	36	28.4 (8.4)	47	ARES (only BAS)	Affective pictures (Happy; Implicit joystick task & explicit rating task)	Greater activation in the middle cingulate cortex, right NAcc and right precuneus for the high BAS group when comparing happy to neutral faces for both tasks. For implicit task, greater activation of the superior orbital/medial gyrus and middle temporal gyrus in high BAS group.	T2* EPI	3T Siemens Trio
Reuter et al., 2004	24	28.2 (5.5)	50	BIS/BAS	Affective pictures (fear evoking, disgusting & erotic)	Disgusting stimuli: positive correlation between BIS and activity in the ACC, PCC, right amygdala and left thalamus. Positive correlation between BAS and activity in the left insula. Fear evoking stimuli: Positive correlation between BIS and activity in the left ACC, left thalamus and right PCC Erotic stimuli: positive correlation between BIS and activity in the left ACC, thalamus, right amygdala, insula, left basal ganglia, left brain stem and the PCC. Negative correlation between BIS and activity in the right OFC. Positive correlation between BAS and activity left hippocampus/parahippocampus	T2* EPI	1.5T Siemens
Simon et al., 2010	24	24.8 (3.2)	46	BIS/BAS	MID task (only gains)	Positive correlation between BAS and activity in the VS and medial OFC during receipt of reward. Positive correlation between BAS and activity in the medial OFC during omission of reward. Negative correlation between BIS and activity in the VS during receipt of reward.	T2* EPI	3T Siemens Trio
Straumen et al., 2012	31	-(-; range between 18-22)	52*	BIS/BAS	Goal priming	No findings for BIS or BAS.	T2* Spiral	3T GE Signa

van Rijn et al., 2016	18	22.1 (1.6)	83	BIS/BAS (Only BAS)	Calorie satisfaction task	Negative correlation between BAS-Drive and activity in the VS, amygdala and ACC when hungry. Positive correlation between BAS-Drive and activity in left caudate when sated.	T2* EPI	3T Siemens Magnetom
Xu et al., 2012	51	29.6 (10)	59	BIS/BAS	DTI	Positive correlation between BAS Fun-seeking and diffusion tensor imaging fractional anisotropy in the left corona radiata and superior longitudinal fasciculus and with mean diffusivity in the left inferior longitudinal fasciculus and inferior fronto-occipital fasciculus	DTI	3T Siemens Trio

GMV = Gray Matter Volume, EPI = Echo Planar Imaging, DTI = Diffusion Tensor Imaging, MPRAGE = magnetization-prepared rapid gradient-echo, FSPGR = fast spoiled gradient echo, FFE = fast field echo, * = weighted

Figure 1


Identification
Screening
Eligibility
Included
Records identified through database searching (n = 14848)
Additional records identified through other sources (n = 2)
Records after duplicates removed (n = 10952)
Records screened (n =10952)
Records excluded (n = 10789)
Full-text articles assessed for eligibility (n = 163)
Full-text articles excluded, with reasons (n = 53)
Studies included in qualitative synthesis (n = 110)
EEG based studies included in sister paper (See Firth, Standen, Sumich & Heym, in prep; n=71)
MRI based studies included as part of the original search (November 2019; n=39)
MRI based studies included in this qualitative synthesis (n=42)
MRI based studies included as part of an updated review (April 2021; n=3)