Chapter 10

The Neuroscience of Personality

Alan D. Pickering and Jeffrey A. Gray
University of London

THE SCIENTIFIC STATUS OF PERSONALITY RESEARCH

Personality occupies a peculiar position within the disciplines of modern psychology. The prevalence of "trait" terminology in everyday language shows how frequently the topic of personality crops up in conversation, and the plethora of do-it-yourself "personality" inventories in popular magazines confirms the well-established place that personality occupies in popular thinking and culture. By contrast, it is our perception that personality research is often accorded a low scientific status by some experimental psychologists and is somewhat underrepresented in top-ranking journals. Much of the responsibility for the status quo must lie with personality research itself. In addition to the inevitable correlational nature of personality studies, the discipline has several other features that tend to cause disdain amongst card-carrying experimentalists. These include the central role of subjective instruments (e.g., self-report measures); the historical tendency to describe personality structure rather than to attempt reductionist explanations; and the strong links between personality and learning theory in the information-processing era. In this chapter we will try to illustrate that technical developments in neuroscience over the last 15 years or so may offer a window of opportunity for personality research to undergo a scientific makeover.

Despite the above difficulties, relating to the scientific status of personality research, there have been several theorists, such as Pavlov and H. J. Eysenck, who have attempted to understand personality—and its psychobiological substrates—via the usual methods of natural science. Now, modern versions of these theories are being given fresh impetus by our abilities to carry our functional imaging studies of the brain, to conduct investigations into the molecular genetics of variations in human neurotransmission, and to interpret these findings in relation to neurally inspired computational models of the relevant processing operations and/or brain systems. One goal of the present chapter is to indicate some of the ways one might try to build a modern, integrated neuroscience of personality.

It is also important to point out that those who have advanced the neuropsychology of human personality have been motivated by an additional desire to cast light on human psychopathology. The fundamental assumption underlying the personality–psychopathology linkage,
and one that underpins our own research, is of
"normal" personality variation lying on a continu-
umum with certain clinical states. The most obvi-
ous example is that of anxiety. Healthy individu-
als vary in trait anxiety, which is simply the
degree to which an individual is generally dis-
posed toward anxious cognitions and behavior.
In this specific example, the continuum model
supposes that certain clinical anxiety disorders are
found in individuals who lie at the high pole of
the "normal" trait anxiety dimension. It has also
long been argued that other disorders (e.g., psy-
chopathy; Lykken, 1957) may occur in individu-
als who lie at the extreme low end of trait anxiety.

Armed with this continuum view of psychopa-
thology there are distinct advantages to inves-
tigating possible psychobiological models of spe-
cific psychopathologies through the testbed of
studies exploring related personality trait vari-
ation within healthy subjects. For example, Pat-
terson and Newman (1993) advance the case for
the study of extraversion as a means of elucidat-
ing the mechanism of disinhibition, which they
believe underpins psychopathy and related disor-
der. In addition to obvious advantages of sub-
ject availability and compliance they note that:
"the behavior of extraverts is the least distorted
by negative life events and comorbidities (e.g.,
substance abuse) ... [and] ... their social disin-
hibition and impulsivity or spontaneity are often
esteemed or adaptive. ... In contrast, psychopa-
thys' often troubled childhoods ... might
modify their expression of the diathesis. Most
extraverted college students have not expe-
rienced the untoward effects of an antisocial life-
style" (p. 718). Claridge (1987) has made analo-
gous arguments for the study of schizophrenic
deficits through the lens of schizotypal personal-
ity trait variation in healthy subjects.

In this chapter we will not attempt a com-
prehensive review of recent neuroscientific find-
ings and theories concerning a range of major
personality dimensions. Instead, we will illus-
trate the use of neuroscience to understand personal-
ity better by concentrating largely on the major
cluster of personality traits that can be referred to
as impulsive sensation seeking (ISS). In this
chapter we will propose a neurobiological
model of these traits by drawing together differ-
ing kinds of neuroscientific findings. A well-
known neuroscientific account of another major
personality dimension—anxiety—has been pre-
sented by one of us previously (Gray, 1982), and
this has been recently updated (Gray & McNaughton, 1996, in press).

**IMPULSIVE SENSATION SEEKING
AND THE REINFORCEMENT
SENSITIVITY THEORY OF
PERSONALITY**

The personality trait of Impulsiveness (or Imp-
ulsivity), in its narrow sense, is usually defined
as a tendency to act rapidly without deliberation
or consideration. However, this trait covaries
with a broader set of characteristics known as
Sensation Seeking, Novelty Seeking, or ven-
turesomeness. Sensation Seeking individuals
tend to engage in behaviors that increase the
amount of stimulation that they experience.
Such behaviors (e.g., participation in dangerous
sports, drug use, etc.) involve seeking out thrills,
danger, and arousal. In this chapter we shall refer
to the whole cluster of related traits as impulsive
sensation seeking (ISS).

ISS traits are typically measured via various
standard self-report questionnaires. Examples
include the IVE (S. G. B. Eysenck, Pearson,
Easterling, & Albopp, 1985), especially its "Impul-
siveness" and "Venturesomeness" subscales;
"Positive Emotionality" from the Multidimen-
sional Personality Questionnaire (Tellegen &
Waller, 1996); various versions of Zuckerman's
Sensation Seeking Scales (e.g., Zuckerman,
1979) and associated subscales; and the Novelty-
Seeking subscale from the Tridimensional Per-
sonality Questionnaire (Cloninger, 1989).

From a theoretical perspective, it has been ar-
gued that Impulsivity, along with Anxiety, repres-
sent fundamental dimensions of temperament
ferences along these dimensions are argued to re-
fect variation in the reactivity, or sensitivity, of
two basic brain systems to their specific classes of
input stimuli. These systems—the "behavioral
inhibition system" (BIS; for anxiety) and "be-
havioral activation system" (BAS; for impulsiv-
ity)—respond to differing kinds of secondary re-
forcing stimuli: the BIS is activated by novel
stimuli and by conditioned stimuli signaling
punishment or frustrative nonreward; the BAS is
activated by conditioned stimuli signaling re-
ward or relief from punishment. We therefore
refer to this account of personality as reinforce-
ment sensitivity theory (RST).

The personality trait label of "Impulsivity,"
when used in relation to the reactivity of a per-
son's BAS, is really a shorthand for impulsive
sensation seeking. An individual with a highly
reactive BAS is proposed to have high scores on
typical ISS inventories, including those listed
above, RST specifically proposes that subjects with high ISS scores (henceforth referred to as "high ISS" subjects) will show very strong responses to those stimuli that activate the BAS (cues for reward or relief from punishment). Gray (1970) argued that the BAS personality dimension was situated in the Extraversion x Neuroticism (E x N) plane of Eysenck's personality system with high ISS subjects being neurotic introverts and low ISS subjects being stable introverts. In subsequent revisions of the Eysenck scales (e.g., EPQ: H. J. Eysenck & Eysenck, 1975) the Impulsivity content is found largely in the EPQ-P scale rather than EPQ-E (Rocklin & Revelle, 1981); and, in male subjects, EPQ-P (partial $R^2 = .20$) explained more variance in IVE-Impulsiveness than did EPQ-E (partial $R^2 = .09$; Ditz & Pickering, 1993). The ISS trait reflecting BAS reactivity seems likely to be indexed at least as strongly by EPQ-P as by any other EPQ scale. Depe & Collins (in press) show that ISS trait measures (which incorporate positive affect) are located on the diagonal between two orthogonal axes, which they labelled Extraversion and Constraint (after Tellegen, 1982). High ISS subjects are characterised by high Extraversion and low Constraint. Given that the low pole of Constraint is anchored by EPQ-P, Depe and Collins' analysis implies that personality trait variation related to BAS reactivity lies along the diagonal between EPQ-E and EPQ-P (not EPQ-E and EPQ-N as originally suggested).

In addition to standard personality measures designed to capture variation in Impulsivity and sensation seeking, Carver & White (1994) have recently developed a set of scales that was intended specifically to index the personality trait variation associated with BAS reactivity. They did this by using items directly related to the psychological effects of rewards and reward cues, along with more general items concerning goal directedness and appetitive motivation. These scales complement the existing published scales similarly designed to index BIS-related personality variation (MacAndrew & Steele, 1991; Torrubia & Tobena, 1984).

The BAS and the BIS compete with one another for control over behavior (Gray & Smith, 1969; Pickering, 1997). When activated, the BAS can be characterized as a "go" system that activates ongoing approach behavior. By contrast, the BIS is a "stop" system that inhibits ongoing behavior and allows further information processing of the environment. These responses are appropriate under BIS-activating conditions in which signals of punishments and/or loss of rewards warn of impending negative consequences. BIS activation is also accompanied by an arousal output that ensures that any actions that are eventually executed (including flight or flight) are carried out with increased force and vigor.

From the perspective of RST, the decision to engage in the dangerous but pleasurable behaviors characteristic of high ISS subjects is viewed in terms of an approach-avoidance conflict, which is resolved by the interactions between BAS and BIS. In a highly BAS reactive (high ISS) subject, the BAS-controlled approach component will tend to predominate, and so these subjects will exhibit a lot of risky, sensation-seeking behaviors. In anxious subjects, with high levels of BAS reactivity, the avoidance component will tend to hold sway, and such subjects will habitually avoid danger and risk.

At this point, we should briefly note some of the psychopathological states that have been related to extremes of the ISS personality dimension. Quay (1988) has hypothesized that childhood behavioral disorders, such as attention deficit disorder with hyperactivity, and conduct disorder, are in part the result of a dysfunctional (overactive) BAS. Impulsivity is a cardinal feature of these childhood disorders. Corresponding disinhibited psychopathologies in adulthood have been similarly ascribed to an overactive BAS (Gorenstein & Newman, 1980) or to difficulties in interrupting or modulating BAS-controlled behavior (Patterson & Newman, 1993).

Finally, we note that RST has mainly been investigated by exploring the behavioral and psychophysiological responses to reward and punishment cues in individuals with different personality trait scores. Subjects' performance on a task is assessed under a control condition in which reinforcements are neither anticipated nor received. This is compared with performance in a condition in which subjects know that their responses will attract explicit reinforcement (usually gains or losses of small sums of money). Despite the existence of many studies, Pickering, Coit, Powell, Kumari, Thornton, & Gray (1997) argued that the theory has not been adequately tested in most, if not all, of the published investigations. It was also pointed out that, within the limitations of the studies, many patterns of findings—from clear supporting evidence through nonsignificant results to clear contradictory evidence—have been reported. Post hoc arguments
have often been used to accommodate awkward
results. Pickering and his colleagues suggest that
the evidence as a whole points to strong links be-
tween personality traits and sensitivity to rein-
forcement, but they argue that it is unclear how
well RST describes those links.

RELATED THEORETICAL
ACCOUNTS

Influential accounts of personality by Cloninger
(Clampinger, Svrakic, & Przybeck, 1993), Zuck-
erman (1991), and Depue (Depue & Collins, in
press) resemble RST in proposing a basic dimen-
sion of personality that shares features with the
BAS-related ISS dimension hypothesized by
RST.

In Cloninger’s theory there are four strongly
biologically determined temperament dimen-
sions and three more environmentally deter-
mined character dimensions. One of the tem-
perament dimensions—Harm Avoidance—is
closely akin to the Anxiety dimension of RST.
By exploring the correlations between Clonin-
ger’s temperament dimensions and those from
the EPQ, Corr, Pickering & Gray (1995) outlined
possible links between BAS function and two of
Cloninger’s other temperament dimensions: Novelty Seeking and Reward Dependence. Novelty Seeking showed the positive asso-
ciations with both EPQ-E and EPQ-P that
Depue and Collins (in press) have shown to be a
consistent feature of ISS traits. These results
were confirmed in a larger study by Zuckerman
and Cloninger (1996).

Subjects with high Novelty Seeking scores are
characterized in a similar way to subjects with a
highly reactive BAS. They are impulsive, ex-
ploratory, fickle, excitable, quick-tempered, and
eXtravagant. Of particular importance for the
present chapter is Cloninger’s proposal that
Novelty Seeking involves genetic differences in
dopaminergic neurotransmission; as discussed
below, there is now direct evidence in support of
this suggestion.

Depue and Collins’s (in press) recent account
differs from those of Cloninger, Zuckerman, and
RST in suggesting that the axes of causal neuro-
biological influence lie jointly with Extraversion
and Constraint, rather than on the ISS diagonal
between these dimensions. Depue and Collins
suggest that ISS traits are emergent from interac-
tions between the fundamental Extraversion and
Constraint dimensions and, as such, would be
expected to have heterogeneous neurobiological
sources of influence. As a result they expect that
research attempting to find neurobiological cor-
relates of ISS traits would tend to produce weak
and inconsistent results. They argue specifically
that evidence for individual differences in
dopaminergic functioning should be more con-
sistently aligned with Extraversion than with ISS
traits. In their review of some of the pertinent
evidence Depue and Collins concede that the
data are pretty indecisive. Depue’s own studies of
prolactin and eye blink indices of D2 dopamine
receptor effects (Depue, 1995, 1996; Depue,
Luciana, Arbisi, Collins, & Leon, 1994), repli-
cated by another group (Netter, Henning, &
Roed, 1996), provide the clearest evidence of
strong associations with Extraversion in the ab-
sence of the significant relationships with ISS
traits or Constraint. These findings must be set
against the evidence, reviewed below, which
finds associations between dopaminergic effects
and ISS or Constraint-like traits, rather than as-
ociations involving Extraversion.

A final related body of research and theory
tems from Newman and his colleagues (Arnett,
Smith, & Newman, 1997; Gorenstein & New-
man, 1980; Patterson & Newman, 1993). These
authors have been less concerned with con-
structing a theory of personality than with build-
ing models of disinhibited pathologies such as
psychopathy. As the earlier quotation from
their work indicates, these authors have felt that
the study of extraverts offers clear insights on
their central question.

The remainder of this chapter will build from
an analysis of the work of Newman and his col-
leagues, which will be considered in some detail.
We will interpret their information-processing
model of disinhibition, and some associated em-
pirical findings, in terms of interactions between
the BAS and the BIS. As we have advocated el-
sewhere (Gray, 1972), this step will lead to the
development of a conceptual nervous system ar-
chitecture for the systems involved. Pickering
(1997) has suggested that conceptual nervous
system models are naturally implemented as
computational neural networks, and so we will
use our knowledge of neural network systems to
help understand the way in which our concep-
tual nervous system might function. In partic-
ular we will consider the effects of systematically
varying network parameters to model personal-
ity trait variation.

The next step will be to look at a range of evi-
dence, from varying neuroscience modalities,
which may provide clues as to where our conceptual nervous system may reside in the brain. Evidence from cell recording studies, work with motivationally disturbed clinical populations, plus developments in neuroimaging and molecular genetics will implicate the mesolimbic dopamine system in BAS function and in ISS personality traits. Next we will try to map the various inputs to, and outputs from, the striatal target cells of the mesolimbic dopamine pathways, onto the conceptual nervous system architecture that we have suggested. By doing this we can construct a more constrained neural model that we hope will be of use in understanding the complex relationships between ISS personality traits and behavior on experimental tasks. We hope, too, that our general approach, illustrated in this chapter, might be an effective framework that could be employed to help integrate the neuroscience data related to other personality traits.

THE PATTERSON AND NEWMAN DISINHIBITION MODEL.

Patterson and Newman (1993) outline a process through which disinhibited individuals (such as extraverts and psychopaths) may exhibit their characteristic impulsive behavioral style. The first stage of this process is the acquisition of a dominant response set for approach behaviors. A very strong approach response set may lead to excessive focus on the behavioral goal, restricting information gathering and consideration of response alternatives, producing perseverative reward-seeking behavior even after environmental contingencies have changed. Patterson and Newman suggest that there are basic differences in the ease with which individuals form approach response sets and the intensity with which the activation of such sets is maintained. They argue that exaggerated responsiveness to reward, of this kind, is responsible for disinhibited behavior. As already noted, they suggest that the relevant individual differences variable is Extraversion.

The second stage of the route to disinhibition occurs when the approach response set is disrupted by an (aversive) event that stalls or prevents further action. Patterson and Newman emphasize the orienting of attention toward the unexpected event and the accompanying increase in arousal. These outcomes are precisely the output functions of the BIS in RST. Further-

more, Patterson and Newman suggest that the key individual differences variable for this processing stage is Neuroticism; Neuroticism is close to the anxiety dimension that RST aligns with BIS reactivity. (It should be noted that although RST has always emphasized the relative closeness of Neuroticism to the anxiety dimension of RST—see Gray, 1970—the issue has been confused somewhat by the simplifying explanatory device of presenting the anxiety dimension as lying on the 45° diagonal between Neuroticism and Extraversion; see Pickering, Cort, & Gray, 1999, for further discussion.)

The third stage of processing according to Patterson and Newman follows immediately after the unexpected disruption of approach behavior. Nondisinhibited individuals use the arousal increment following disruption to make an effortful switch from automatic processing under the reward expectancy to controlled processing of the circumstances surrounding the unexpected interruption. Once again, this precisely resembles the functional account of behavioral inhibition that we have offered (for example, see Pickering, 1997). Patterson and Newman propose that disinhibited individuals often fail to make the automatic-to-controlled processing switch and so show weak modulation of their overt goal-directed behavior and the underlying response set. From the perspective of RST, disinhibited individuals display functionally impaired behavioral inhibition. Patterson and Newman refer to the individual differences at this stage as being differences in "response modulation bias" and relate this bias to Extraversion. It seems likely that failures of response modulation (Stage 3) in extraverts might be responsible for their proposed tendency strongly to maintain the activation of an approach response set (Stage 1), although the acquisition of a response set might logically be distinguishable from modulatory processes involved in its maintenance.

The fourth element of Patterson and Newman’s account describes an associative deficit that usually follows disinhibition of appetitive behavior. They suggest that weak response modulation often leads to a failure to pause and process the cues that, through learning, could serve as early warning signs of the originally unexpected interruptions of reward-seeking behavior. Disinhibited individuals therefore typically show reduced reflectivity following punishments, and the resulting impairment of learning skews response repertoires toward active, goal-directed behavior. Interestingly, Patterson, Kosson, &
Newman (1987) have shown that extraverts do learn from their mistakes when they are forced to pause after corrective feedback, presumably because this allows them time for the kind of reflective processing described above, time that their habitual behavioral style does not usually allow.

A CONCEPTUAL NERVOUS SYSTEM MODEL OF BAS–BIS INTERACTIONS

We have pointed out the close similarities between parts of the above account and the central ideas of RST: similarities that Newman and his colleagues explicitly acknowledge. Following Arnett, Smith, and Newman (1997), we find it helpful to relate the disinhibition model to RST using a diagram; see Figure 10.1. This figure is based on the original diagram from Gray and Smith (1969) and shows multiple outputs from both the BAS and the BIS. Each system responds to its characteristic motivational inputs by producing a modulation output (which inhibits the other system) and an output that has a functionally excitatory effect on a general arousal system. The third output of each system affects response selection and control mechanisms: the BAS output activates and the BIS output inhibits any response habits elicited by other stimuli in the environment.

Figure 10.1 represents a simple conceptual nervous system architecture for the BAS and BIS, and their associated personality traits. Next, we need to understand how such an architecture might function. As already noted, this process may be facilitated by interpreting Figure 10.1 as if it were the architecture of a neural network. The simplest version of RST would propose that, in response to a learned cue signaling reward, each of the outputs from the BAS would be stronger for a high ISS subject than for a low ISS subject. (Analogous statements could be made for the BIS and Anxiety.) If one were to construct a neural network model with the basic architecture of Figure 10.1, the simplest version of RST would model ISS traits by allowing the threshold function controlling the output from BAS “cells” to vary across individuals (high BAS reactivity = high ISS = low BAS output threshold). Similarly, trait Anxiety would be modeled by varying the threshold controlling BIS output. It would logically be possible to model variations in the sensitivity of the BAS or BIS to their respective input stimuli in terms of variations in the synaptic efficiency (or weights) of the input pathways to each system. Indeed, Pickering (1997) used this method as a computational convenience. However, for reasons made clear below, we do not advocate this possibility here.

According to RST, Extraversion is a personality dimension that emerges from the interplay between BAS and BIS. The personality traits associated with BAS and BIS reactivity (ISS and Anxiety, respectively) are therefore argued to be causally and biologically more fundamental than Extraversion. As a result, one would not seek to model Extraversion by varying one specific feature within a framework like that in Figure 10.1. Instead, Extraversion would be modeled by simultaneous variations in features of both BAS and BIS. In RST, extraverts are considered to be relatively high in Impulsivity (high BAS output) and also relatively low in Anxiety (low BIS output). We (Pickering, 1997) have previously used a neural network to explore the equilibrium state of the mutually inhibitory BAS and BIS systems.

---

**FIGURE 10.1.** A schematic representation of the inputs to and outputs from the behavioral activation system (BAS) and behavioral inhibition system (BIS). The arousal system is depicted as affecting response selection mechanisms, but it is likely to have a direct effect on the response systems. Pathways are functionally excitatory except where minus signs denote functionally inhibitory effects. Learned inputs are denoted by pathways ending in rounded arrowheads. In this chapter we argue that inhibition of the BIS by the BAS may be insignificant.
when both receive inputs. For an extravert, under the simple version of RST, our previous simulations showed that the outputs from the BAS would be active while the outputs from the BIS would be inactive. This type of model does generate an approach (BAS) dominated behavioral style, consistent with the actions of disinhibited individuals, but it does not fit easily with a number of empirical findings from Newman's laboratory.

The problem for our neural net implementation of BAS–BIS interactions occurs when a punishment cue is experienced during appetitively motivated behavior (stage 2 of Patterson and Newman's disinhibition model). For the BAS-reactive, BIS-unreactive (extravert) subject, the neural net model predicts that there will be no significant BIS outputs and thus little observable response to the punishment cue. The neural net model also predicts that the behavior of the BIS-reactive, BAS-unreactive (introvert) subject, by contrast, will be affected by the combined effects of the inhibition and arousal outputs of the BIS. However, we have pointed out (see Pickering, Diaz, & Gray, 1995) that it might be hard to determine what the combined effects of these opposing outputs would be. These predictions are at odds with the findings (Nichols & Newman, 1986; Patterson et al., 1987) that show that extraverts' response times (RTs) are facilitated following punishment relative to RTs following reward, with the opposite pattern being obtained for introverts. This punishment-related facilitation of RTs in extraverts implies the existence of an active output from the BIS, in response to the punishment cue, even for an extraverted subject who is viewed as being BIS-unreactive.

In order to explain extraverts' RT facilitation following punishment, within the context of Figure 10.1, it is necessary that the BIS can remain activated even when the BAS is activated more strongly. Such a state of affairs will not arise with the strong competitive interactions between BAS and BIS that we have previously employed (Pickering, 1997). It could occur, however, if there were no (modulation) output from the BAS that acted on the BIS directly. In this case activation of the BAS (and thus the level of each BAS output) would be a function of the activating inputs and the inhibitory modulation received from the BIS, whereas BIS activation (and outputs) would be solely determined by its activating inputs. BIS activation would therefore not be driven to zero by inhibitory modulation from the BAS even under conditions that activate the BAS more strongly than the BIS.

How would this revised model explain facilitation of RT in extraverts following punishment cues? The net effect of the BIS-activating cue would result from the facilitatory effects of the BIS arousal output opposed both by the reduction in BAS activation produced by the BIS modulation output and the direct effect of the BIS inhibition output on response selection, acting in opposition to the effects of the BAS activation output. In an extravert or high ISS subject there is some degree of BIS reactivity. Under RST, Neuroticism is aligned much more closely with BIS reactivity than Extraversion, and ISS traits are hypothetically orthogonal to the BIS dimension of anxiety. Therefore, in Extravert or high ISS subjects, a BIS-activating cue will produce a degree of BIS activation. In the modified account of RST, just given, this BIS activation will not be suppressed by the much stronger BAS activation (for extraverts or high ISS subjects) produced by any concurrent BAS-activating cues. The resulting modest BIS modulation output will not have much effect on BAS activation, and the modest BIS inhibition output will not have much success in opposing the effects of the strong BAS activation output on response selection. However, the modest BIS arousal output will be able to express its effects on responses directly and unopposed, leading to an increase in response speed. By comparison, introverted or anxious subjects will have much greater BIS reactivities (as well as reduced BAS reactivities), and so the BIS modulation and inhibition outputs may achieve a marked interference with any ongoing BAS-mediated effects. The overall effect of a punishment cue on appetitively motivated behavior will be determined by these BASS-opposing effects in combination with the effects of the BIS arousal output. An increase in RT may therefore be observed in introverts in response to a punishment cue.

We have now completed our conceptual nervous system analysis of a possible gross neural architecture for the BAS, the BIS, and their interaction. We have seen that an understanding of mutually inhibitory, competitive dynamics between systems, gathered from experience with neural network models, has led to a reformulation of RST to accommodate the findings of Newman and colleagues. In terms of Figure 10.1 we make a simple modification: to drop the arrow denoting direct inhibition of the BIS by the BAS. This reformulation also represents a more
detailed specification of the response modulation account of disinhibition suggested by Patterson and Newman. We now turn to evidence relating to the neurobiology of the BAS more directly. By exploring real neural networks in the brain, and how they function under appetitive motivation, we may be able to map the abstract representations of Figure 10.1 onto actual wetware in order to construct a more constrained and realistic model.

THE NEUROBIOLOGY OF THE BAS
Evidence for Dopaminergic Involvement in Appetitive Motivation

We have previously given a thumbnail sketch of the neurobiology of the BAS (Gray, 1987). A central role for dopaminergic neurotransmission in BAS function is mandated given the strong evidence implicating mesolimbic and mesocortical dopaminergic pathways in reward-directed behavior (Bozarth & Wise, 1981; Robbins & Everitt, 1996). This is not to argue that dopaminergic neurotransmission in mesolimbic pathways is exclusively linked to positive incentive motivational effects, as we have emphasized elsewhere (Gray, in press; Gray, Kumari, Lawrence, & Young, in press). It is clear, for example, that aversive stimuli increase mesolimbic dopaminergic neurotransmission (see Salomone, 1994, for a review). It may therefore be more complete to argue that the common denominator underlying the capacity of a stimulus to elicit dopamine release in mesolimbic pathways is its salience (see Gray et al., in press). Nonetheless, we argue here that one type of salience (and hence one route to mesolimbic dopamine release) is a product of the action of the BAS. A major goal of this chapter is to highlight the possible input and output pathways of this system.

A particularly pertinent series of studies has been summarized by Schultz, Romo, Ljungberg, Mirenowicz, Hollerman, & Dickinson (1995). They report cell recordings from monkey dopamine neurons in the substantia nigra (SN) and ventral tegmental area (VTA) that reveal that dopaminergic activity increases in response to primary rewards. After training, however, the cells respond to conditioned stimuli (CSs) that predict the primary reward rather than to the primary reward itself. Such CSs, according to RST, represent one of the classes of stimuli that activate the BAS.

Houk, Adams, and Barto (1995) offer an interpretation of the results described by Schultz et al. that is entirely consistent with RST. In the schematic neural architecture of Figure 10.2, an appetitive unconditioned stimulus (US) leads to increased firing of SN or VTA dopaminergic neurons. Dopamine release at the striatal target cells (S in Figure 10.2) of these dopaminergic neurons is argued to be an additional, critical factor involved in a special form of long-term potentiation (LTP). This LTP is the basis of conditioning in the glutamatergic cortical afferents carrying information about CSs to the striatal cells. After conditioning, a CS is able to elicit robust firing of the striatal neurons in the absence of the US. The outputs from the striatal cells send feedback signals that control the dopaminergic output from the SN/VTA neurons. A CS can produce two types of striatal feedback signals: one indirectly leads to a functional excitation of dopaminergic firing (by inhibition of the inhibitory inputs from various nuclei to the SN/VTA neurons); Houk et al. (1995) argue that there is also a much slower, direct signal (not shown in Figure 10.2) that inhibits dopaminergic firing and so opposes the increase produced by the ensuing US. In this chapter we are going to emphasize the indirect pathways. The other cells receiving dopaminergic input include the prefrontal cortex (PFC in Figure 10.2). These regions are involved in selection and control of such behavioral outputs as learned stimulus-response (S-R) habits. As well as a possible role in modulating learning in these pathways, dopaminergic transmission may also play a direct role in selection of the stimulus inputs that undergo learning (Schultz et al., 1995) and in the psychomotor activation of the selected behavioral outputs (Wickens, 1993).

In terms of RST, the outputs from the striatal cells, elicited in response to an appropriate CS, correspond to the outputs of the BAS. Impulsive sensation seeking subjects, whom RST supposes to have a reactive BAS, should therefore produce strong striatal feedback signals in response to a CS that has previously been associated with reward. We noted earlier that RST suggests that this increased BAS output results from a lowered output threshold of the cells concerned. The Houk et al. model, summarized in Figure 10.2, describes a form of classical conditioning in cortico-striatal pathways by which initially neutral CSs can become a secondary positive reinforcer and elicit conditioned dopaminergic cell firing.
From the foregoing account, a CS previously associated with reward will, via the indirect striatal output routes, initially elicit high levels of dopaminergic firing in an impulsive subject. Below we will develop a more detailed neural model of the BAS, building on the ideas sketched to date. We will suggest that these striatal output signals, and their associated increase in dopaminergic firing, can produce the behavioral activation effects ascribed by RST to the BAS. We will also make a specific suggestion for a possible neurochemical basis for the increased striatal outputs of an impulsive sensation seeking subject. At this point we should also reiterate our earlier statement: namely, that other kinds of stimuli can elicit dopamine release in striatal cells. In the more complete model, presented below, we will briefly suggest how aversive and other events can elicit dopamine release in the ventral striatum. Some of these effects will be interpreted as resulting from the interaction of BIS outputs with BAS processing. Emphasizing this point is important so that the reader does not mistakenly infer any simple equivalence between dopamine release and appetitive motivation. We have stated elsewhere that such a view is at odds with a great deal of evidence (Gray et al., in press).

Other evidence for DA involvement in BAS function comes from studies of patients with clinical abnormalities of appetitive motivation. Powell and her colleagues have developed a simple experimental measure of reward motivation, the CARROT (Card Arranging Reward Responsiveness Objective Test), suitable for use with clinical groups. The CARROT is a repeated-measures test in which subjects are required to perform a very simple card sorting task as quickly as possible on four separate consecutive trials (T1–T4). On one trial (T3) the subjects are offered a financial incentive for fast sorting (10 pence for every five cards sorted); and their sorting rate on this rewarded trial is compared with their sorting rate in nonrewarded trials conducted either side of the rewarded trial (T2 and T4) to yield a "reward responsiveness" index. These researchers administered the CARROT to 54 patients with organic brain injury, some of whom were characterized by clinically significant impairments of appetitive motivation (Adawwi, Powell, & Greenwood, 1998). The reward responsiveness index correlated strongly with independent clinical ratings of motivation during therapy sessions (r = .64, p < .001), and
this reflected neither a general effect of motor slowing (speed in the nonrewarded trials was uncorrelated with motivation) nor generalized intellectual deterioration. In a parallel study (Powell, Al-Adawi, Morgan, & Greenwood, 1996), 11 of the patients with severe motivational impairment were treated with a D2 dopamine agonist, bromocriptine, after they had been stable over two repeated baseline (i.e., drug-free) assessments. There were highly significant improvements at low doses of the drug, both in clinically rated motivation and in the reward responsiveness scores from the CARROT. The effect of bromocriptine was specific to the reward responsiveness index as there were no effects on sorting speed on nonrewarded trials. The CARROT therefore appears to be a simple measure of the effects of reward cues that shows both ecological validity and dependence on dopaminergic neurotransmission.

The next study used the CARROT to test Muslim smokers abstaining from cigarettes during daylight hours throughout Ramadhan (Al-Adawi & Powell, 1997). The subjects were given the CARROT after several hours' abstinence and then again shortly after smoking in the evening. The smokers compared with nonsmoking Muslim controls. When abstaining the smokers showed virtually no reward responsiveness on the CARROT, but they showed a subnormal effect when tested immediately after one cigarette. The controls' levels of reward responsiveness were higher on the first testing occasion and did not change at the second testing point. As with the brain-injured patients, the effect on reward responsiveness was independent of speed in the nonrewarded trials. Because nicotine is known to stimulate dopamine release in the brain directly, via nicotinic receptors on dopaminergic neurons, and because withdrawal from various addictive drugs has been shown to be associated with abnormal functioning in dopaminergic brain circuitry (see Al-Adawi & Powell, 1997, for references), the results are again consistent with appetitive motivational effects in the CARROT task being mediated by brain dopaminergic activity.

Evidence from clinical populations, data from functional neuroimaging investigations, and findings from molecular genetic association studies.

Indirect Evidence

There are clinical conditions in which alterations in the frequency of Impulsive and Sensation Seeking behaviors are observed and in which there is evidence of altered dopamine function. These conditions provide indirect evidence linking ISS personality traits with dopaminergic neurotransmission. Attention deficit disorder with hyperactivity in children is one of the major behavioral disorders of childhood and is characterized, inter alia, by impulsiveness. The most commonly prescribed medication for this condition in the US is methylphenidate (Kwan, Tisley, & Lepper, 1995). Methylphenidate acts by inhibiting the dopamine transporter to which it binds specifically (Ding, Fowler, Volkow, Logan, Gatley, & Sagano, 1995). In addition, we have already noted that Quay (1988) has characterized attention deficit disorder and conduct disorder in terms of a disturbance to the functioning of the BAS and its interaction with the BIS. In a general review of the genetics of childhood psychopathology, Alsobrook and Pauls (1998) note the evidence linking Gilles de la Tourette's syndrome—which is also characterized by marked deficits of impulse control—to D2 and D4 dopamine receptor functioning.

In adults, clinicians have anecdotaly observed an association between Parkinson's disease and personality characteristics at the low pole of the ISS dimension (i.e., stoicism, industriousness, and inflexibility), both premorbidly and after the onset of symptoms. Menza and colleagues (Menza, Forman, Goldstein, & Golbe, 1990; Menza, Golbe, Cody & Forman, 1993) have documented low levels of Cloninger's Novelty Seeking in Parkinson's disease patients and have argued that damage to the mesolimbic dopaminergic system in Parkinson's disease is responsible for the patients' characteristic (low ISS) personality profile.

Neuroimaging Investigations

There have been relatively few studies that have attempted to use functional neuroimaging to study personality traits. Our own single photon emission tomography (SPET) study in a small group of healthy volunteers (N. S. Gray, Pickering, & Gray, 1994) used a specific radioligand...
for dopamine D2 receptors (\([^{125}I]\)IBZM). We correlated the left and right hemisphere measures of ligand binding in the basal ganglia with scores on the EPQ. We found significant negative correlations between the P scale from the EPQ with the D2 binding index in each hemisphere, but no significant associations with other personality measures from the EPQ. The binding index, lower in subjects with high EPQ-P scores, is an index of D2 receptor density. There are some noteworthy aspects to these findings.

First, in this chapter we have emphasized the widely held view that EPQ-P is an index of antisocial ISS personality traits and does not satisfy Eysenck's original intention that this scale should index Psychoticism (i.e., a general tendency to psychotic-like thoughts and behaviors). Our earlier analysis of the recent review by Depue and Collins (in press) was that ISS personality traits are usually located along the diagonal running from high EPQ-P and high EPQ-E (high ISS) to low EPQ-P and low EPQ-E (low ISS). The current scanning findings are consistent with this analysis if one assumes that the causal (biological) personality axis, related to variations in dopaminergic neurotransmission, lies along the ISS diagonal rather than with EPQ-E or EPQ-P. Either of these latter dimensions may then act as a proxy for the fundamental ISS traits, with which they are correlated, and reveal associations with dopaminergic indices (such as SPECT binding). As Depue and Collins point out, these indirect associations will be weaker, and more inconsistent across studies, than associations with personality measures that tap into the causally significant dimension directly. This expectation of weak and inconsistent effects can explain why there were no EPQ-E correlations in our scanning study, and at the same time why Depue's studies of psychophysiological dopaminergic markers (see above) were associated selectively with Extraversion and not Constraint (a dimension that is approximately the inverse of EPQ-P). By contrast, Depue and Collins's claim that Extraversion is the true dopaminergic personality dimension cannot explain the results obtained by N. S. Gray et al. (1994).

Second, a research group in Sweden (Farde, Gustavsson, & Jonsson, 1997) has independently reported on the personality correlates of D2 receptor binding in a larger group of healthy volunteers. Receptor density (in right and left striatum combined) was measured using positron emission tomography (PET) with a different radioligand, and personality was assessed via the Karolinska Scales of Personality (KSP). Significant negative correlations were obtained for the dimensions of Detachment and Irritability, which index some of the same personality facets as EPQ-P. The correlations with other scales from the KSP were insignificant and were not reported; in particular it would have been interesting to know the relationships with the Impulsiveness and Monotony Avoidance scales, which more directly tap into the hypothetically critical ISS traits.

Finally, a further PET study in a small group of Parkinson's disease patients (Menza, Mark, Burn, & Brooks, 1995) looked at the relationship between Cloninger's Novelty Seeking and striatal uptake of \([^{125}I]\)dopa. Uptake of the ligand in the left caudate, but not other measured regions, was significantly correlated with Novelty Seeking. These workers related these findings to their earlier studies (Menza et al., 1990, 1993) which had shown low levels of Novelty Seeking in Parkinson's disease patients.

**Molecular Genetic Association Studies**

Recent reports have provided the first evidence, in human personality research, of an association between scores on a specific personality inventory and structural variations in the subjects' DNA. This research is germane to the present chapter as the inventory concerned (Cloninger's Novelty Seeking) measures aspects of ISS personality and the gene codes for the dopamine D4 receptor (Benjamin et al., 1996; Ebstein et al., 1996). This research is described in more detail in Chapter 9 by Plomin and Caspi and so will be only briefly summarized here.

The dopamine D4 receptor (DRD4) marker consists of alleles with from 2 to 8 repeats of a 48 base-pair sequence in exon III of the gene on chromosome 11 that codes for the dopamine D4 receptor. The number of repeats changes the length of the third cytoplasmic loop of the receptor. Various in vitro studies (e.g., Asghari et al., 1994) have shown that the shorter alleles (2 to 5 repeats) are to a receptor that is more efficient in binding dopamine than the longer alleles (6 to 8 repeats). For this reason, DRD4 genotypes have usually been analyzed by comparing individuals who have two short alleles (about two-thirds of genotypes) versus one or two long alleles (one-third of genotypes).

In the original studies individuals with at least one long-repeat DRD4 allele showed significantly higher Novelty Seeking scores than indi-
individuals without a long-repeat allele. The other three Cloninger temperament scales (Reward Dependence, Persistence, Harm Avoidance) showed no significant differences between the two groups. These findings have been subsequently replicated (Elstein et al., 1997; Ono et al., 1997). The positive findings must be considered in light of four studies that failed to find significant associations. However, two of these negative studies showed trends in the expected direction (Johansson et al., 1997; Vandenberghe, Zonderman, Wang, Uh, & Costa, 1997). Two other studies showed no association (Malhotra et al., 1996; Pogue-Geile, Ferrell, Deka, Debski, & Manuck, 1988).

The nature of the possible links between these molecular genetic findings and RST poses some interesting questions. The subject characterized by RST as reacting strongly to reward cues might tend to possess the long D4DR allele associated with higher Novelty Seeking scores. This possibility would be consistent with the similarities in personality profile of a BAS-reactive subject (according to RST) and a subject scoring highly on Cloninger’s Novelty Seeking. Earlier in this chapter we suggested that high levels of BAS reactivity would lead to increased dopaminergic firing in response to CSs associated with reward. These ideas must be considered in relation to the in vitro findings that suggest that the long D4DR alleles may be associated with less efficient dopaminergic transmission. These latter findings are consistent with the idea that subjects with the long D4DR alleles seek out high levels of the kinds of environmental stimulation likely to increase dopaminergic activity, in order to compensate for their naturally hypofunctioning system. Given the action of opiates on the mesolimbic dopamine pathways in the brain (Di Chiara, Aquas, & Carboni, 1992), this account could explain the findings of three studies that have found high frequencies of long D4DR alleles among heroin addicts (e.g., Li et al., 1997). There is, however, some tension between suggesting that impulsive sensation seeking subjects have increased dopaminergic firing in response to reward cues and at the same time noting evidence possibly indicating that some of their receptors do not bind dopamine very effectively.

The most straightforward resolution to this paradox is to note that the D4 dopamine receptor is part of the “D2-like” family of dopamine receptors (Jaber, Robinson, Missale, & Caron, 1996). D2 dopamine receptors act to inhibit the depolarizing effects of cortical signals on striatal neurons by a presynaptic action on the corticostriatal terminals (e.g., Hsu, Huang, Yang, & Gean, 1995). In the earlier discussion of Figure 10.2, it was suggested that the high ISS subject would have a lowered threshold for output from the striatal cells receiving cortical inputs from CSs associated with reward. It is therefore a natural step to conceive of the inhibitory D2-like dopamine receptors as setting this threshold for striatal output in response to cortical stimulation. Assuming a similar mode of action for D4 and D2 receptors, it follows that when D4 receptors are less efficient a lower striatal output threshold should result. In this way, the long D4DR allele might be associated with the hypothesized higher striatal output of high ISS subjects. This in turn would lead to greater firing of the dopaminergic cells in the VTA/SN. These cells, particularly those of the VTA, have very diffuse projections to many important neural structures, including prefrontal cortex and amygdala. It will be suggested below that greater excitatory dopaminergic effects at these other target sites (perhaps mediated by D1-like receptors) may be partially responsible for the high levels of behavioral activation characteristic of high ISS subjects.

This speculative account is consistent with a recent study (Tarazi, Campbell, Yeghiaian, & Baldessarini, 1998) that concluded that D4, but not D1 or D2, receptors are found on presynaptic corticostriatal afferents. However, there is evidence from in vitro hybridisation studies that D4 receptor mRNA expression is very low in striatal regions (see Jaber et al., 1996) and some studies with D4-selective radioligands have revealed no high affinity binding in human striatum (Primus et al., 1997). The suggestion that an inhibitory D2-like mechanism determines the striatal output threshold also fits with our own PET data reviewed earlier. The high ISS subjects were found to have lower D2 binding in the striatum. This might indicate lower D2 receptor density, which might in turn be expected to result in reduced dopaminergic inhibition and hence greater striatal output.

In addition to the D4DR marker, just discussed, polymorphisms in a number of other genes may have a role in ISS personality traits. Examples include polymorphisms of the dopamine D2 receptor and dopamine transporter genes. The former has been linked to personality in cocaine addicts (Compton, Anglin, Khalsa-Denson, & Paredes, 1996); the latter has been
linked to attention deficit disorder (Alsobrook & Pauls, 1998), a condition that we have already noted is characterized by impulsivity.

Some New Data

The evidence reviewed earlier suggests that (1) the CARROT task is a simple measure of the appetitive motivational processes related to BAS functioning; (2) it has successfully revealed deficits in the responses to reward cues of patients with altered motivational processes (brain injured; smokers); and (3) performance on the task may be responsive to changes in brain dopaminergic transmission (bromocriptine study). We (Pickering et al., submitted) therefore set out to explore the relationship between performance on the CARROT task and the ISS personality traits hypothesized (under RST) to be especially sensitive to reward cues. We then carried out a subsequent study addressing the possible associations between CARROT performance and genetic variations at the DRD4 locus.

CARROT performance was measured in 167 young (mostly undergraduate) subjects. Several significant relationships with CARROT performance were found with subscales from each of the ISS questionnaires that we used: Extraversion from H. J. Eysenck and Eysenck's (1975) EPQ; Zuckerman's (1979) Sensation Seeking Scale; S. B. G. Eysenck, Pearson, Easting, and Allsopp's (1985) IVE scales; plus Carver and White's (1994) BIS/BAS scales. On the first (baseline) CARROT trial and/or the second (nonrewarded) trial, subjects scoring high on the above questionnaires showed a significantly higher rate of card-sorting. Card-sorting rate increased significantly between the first and second trial, but this was not associated with any of the personality measures. Subjects who scored low on the personality measures, relative to those with high scores, had significantly greater increases in card-sorting rate from the second to third (rewarded) trial, and significantly greater decreases from the third to the fourth (nonrewarded) trial. The data are shown in the upper panel of Figure 10.3 (see next page) with the sample subdivided about the median of the Impulsiveness subscale of the IVE (S. G. B. Eysenck et al., 1985).

In a subsequent study with 47 subjects we also looked at CARROT performance as a function of DRD4 allele length. Long-allele subjects (N = 13) sorted cards significantly faster in both the first and second CARROT trials. They also showed a significantly smaller increase in sorting rate on the third rewarded trial relative to the second trial. The results are depicted in the lower panel of Figure 10.3 where the similarities to the findings for personality measures are obvious. Although the gene-personality associations discussed earlier are being intensely researched, these pilot results are the first to link a specific experimental measure of human behavior to variations in genetic structure. It may be noteworthy that these results were obtained in a sample smaller than those used in gene-personality association studies. This might imply that genetic markers (such as the D4DR alleles) have a stronger influence on specific behaviors or processes than on broad personality traits, such as Novelty Seeking. Broad traits are thought to reflect the influence of a collection of processes, some of which would relate to any one specific genetic marker.

In both these studies, it appears that the ISS (or long allele) subjects, whom RST would predict to be the most sensitive to reward cues, actually showed the smallest response to the reward cues present during the third trial. However, this aspect of these studies appears to be difficult to interpret unequivocally. There seems to be a ceiling on card-sorting rate at about 1.25 cards/second. As subjects become more practised at the task across several trials, they all tend to increase their card-sorting rate. Hence subjects who start at a faster rate, for whatever reason, tend to reach the performance ceiling in fewer trials. It seems likely that subjects with high scores on ISS personality traits and/or long D4DR alleles (who show clear evidence of faster initial sorting rates) may be approaching the performance ceiling after the second trial and are therefore able to show little improvement on trial 3, which coincidentally happens to be the rewarded trial. Subjects with low ISS trait scores and/or short D4DR alleles (who have slower initial sorting rates) are able to show improvements on trial 3 that are less affected by any ceiling effect.

We are still left with the important observation of baseline differences in sorting rate. It is possible that they have nothing to do with the processes with which this chapter has been concerned (responses to reward cues and associated dopaminergic neurotransmission). A more interesting possibility, suggested by Pickering (1997), is that the initially faster rate of card-sorting itself may reflect differences in responsiveness to reward cues. The argument rests on the sugges-
FIGURE 10.3. Mean card-sorting rates during the four trials (T1–T4) of the CARROT task. *Upper panel:* subjects subdivided according to scores on the Impulsiveness subscale from the IVE (S. G. B. Eysenck et al., 1985). *Lower panel:* subjects subdivided according to the presence of at least one long allele (7 or 8 base-pair repeats) in the D4 dopamine receptor gene.

tion that, even in the baseline trial, covert cues of possible rewards are present (e.g., there is the prospect of the subject gaining social reinforcement from the experimenter for performing the task well). If this is accepted then it would be those subjects with a reactive BAS (i.e., high ISS subjects) who would display behavioral activation effects in response to these covert reward cues. Their card-sorting performance would thus be expected to start at a faster level.

To address these interpretations we carried out a third CARROT study in 60 undergraduate subjects to whom we had also given Cloninger’s Tridimensional Personality Questionnaire. The Novelty Seeking (NS) score from this scale provided a measure of ISS personality. The CARROT task was modified so that the financial incentives were given on the second trial. It was hoped that this would allow us to see the effect of the reward cues, in relation to NS, uncomplicated by ceiling effects. There was a nonsignificant positive correlation between NS and baseline sorting rate. However, there was a significant positive correlation between NS and the increase in sorting rate between the baseline and the rewarded trial. This finding is in accordance with the predictions of RST (high ISS subjects should show the greatest behavioral activation in response to reward cues). Furthermore, it lends weight to the idea that the differences in
baseline sorting rate between high ISS (long D4DR allele) and low ISS (short D4DR allele) subjects may reflect differential responses to covert reward cues present on the baseline trial.

DEVELOPING AND ELABORATING THE NEURAL MODEL OF THE BAS

In Figure 10.1 we sketched a conceptual nervous system architecture for the BAS, the BIS and the interactions between the two systems. We suggested that, in order to accommodate findings by Newman and colleagues, the modulation output from the BAS (i.e., the output that inhibits BIS activity) should be omitted. In Figure 10.2 we began to fill in details of a possible neural network that might form the substrate of the BAS. We suggested that the output threshold of striatal cells might vary systematically as a function of ISS personality traits. Specifically, a low threshold would be characteristic of a subject with high levels of ISS traits, and this would generate a greater degree of BAS output for a given BAS input (such as a secondary positive reinforcer). In this way the high ISS subject would have a highly sensitive/reactive BAS, in keeping with the account offered by RST. Finally, we suggested that the low output threshold from the striatum might be a function of inefficient inhibitory (D2-like) dopaminergic synapses on striatal neurons. The functional properties of these dopaminergic synapses might in part be coded for by geneic variations, such as the polymorphisms that affect the structure of the D4DR and which appear to be related to ISS traits.

In order to develop our model, we must elaborate the neural architecture of Figure 10.2 to locate the sites at which the BAS outputs affect behavior and to locate the neural pathways for BAS–BIS interactions. Thus far we have not differentiated between the dorsal (caudate–putamen) and ventral (nucleus accumbens) parts of the striatum. This was because the cell recording studies summarized by Schultz et al. (1995) revealed no differences when recording from dopaminergic cells in the SN (which project to caudate–putamen) or the VTA (which project to nucleus accumbens, NAcc). It is clear, however, that NAcc (and in particular the shell subregion of NAcc) has the appropriate kinds of connections to underpin the BAS functions and BAS–BIS interactions of Figure 10.1 (see Depue & Collins, in press).

Drawing on the work of Swerdlow and Koob (1987), we have previously emphasized the outputs from NAcc via the ventral pallidum in controlling the execution of motor programs (Gray, Feldon, Rawlins, Hemsley, & Smith, 1991). As described by Schultz et al. (1995; see above), NAcc output may be triggered by conditioned stimuli associated with reward (denoted "BAS input" in Figure 10.4). We have argued that greater output from NAcc (resulting from weaker dopaminergic inhibition) is related to high scores on BAS-reactive ISS personality traits. As shown in Figure 10.4, the outputs from NAcc are inhibitory in nature (mediated by the neurotransmitter gamma-aminobutyric acid, GABA). The NAcc output produced by a BAS input stimulus would therefore lead to reduced activity in the ventral pallidum (VP). In turn this would produce reductions in the inhibitory (again GABAergic) outputs from VP to NAcc. For our present purposes there are two important effects of reduced VP output: The firing rate of the dopaminergic cells of the VTA would increase, and the reverberatory feedback between prefrontal cortex (PFC) and the dorsomesial nucleus of the thalamus (DMNT) would be facilitated. All these effects, in the chain of neural events triggered by a BAS activating input, are expected to be larger in subjects with high ISS trait scores relative to subjects with low ISS scores.

The PFC–DMNT loops are involved in response selection and control, directing the execution of the specific steps in a selected response sequence, and these specific sensorimotor steps are themselves encoded in corticostratial pathways within the caudate motor system. (The caudate motor system is centered on the dopaminergic pathway from SN to caudate–putamen; see Gray et al., 1991.) The PFC–DMNT loop is represented schematically in Figure 10.4 in terms of competitive interactions between neurons controlling different response outputs (R1, R2, etc.). When a conditioned stimulus associated with reward elicits output from NAcc, we have noted that this will give rise to an increase in dopaminergic firing in the VTA. This will subsequently lead to an increase in the dopaminergic inhibition of NAcc firing. This increased inhibition at NAcc therefore acts to provide a natural temporal limit on the NAcc response to BAS input stimuli. A BAS activating stimulus is therefore expected to exert a phasic burst of behavioral activation.

In Figure 10.4, the only activation output from the BAS that is depicted is the projection
FIGURE 10.4. A schematic neural architecture for the behavioral activation system (BAS) and its interactions with the behavioral inhibition system (BIS). A BAS output to the arousal system and the BIS inhibition output are not shown. The critical neural loci are as follows: the ascending dopaminergic projections from the ventral tegmental area (VTA) to nucleus accumbens (NAcc); the ventral pallidum (VP); the dorsomedial nucleus of the thalamus (DMNT); and the prefrontal cortex (PFC) response control system, which selects between available responses (R1, R2 etc.). The BIS outputs may derive from amygdala, entorhinal cortex, and subiculum. Pathways are excitatory except where minus signs denote inhibitory connections. Rounded arrowheads indicate modifiable synapses; double-headed arrows indicate reciprocal connections. The BIS modulation output (BMO) is depicted by a modulatory synapse to reflect its influence on the inhibitory dopaminergic effects of the VTA-NAcc pathway (see text for details). US, appetitive unconditioned stimulus; CS, conditioned stimulus associated with US; BAO, BAS activation output.

From NAcc to VP. However, the VTA also sends dopaminergic projections to the PFC. This projection may serve as an additional BAS activation output pathway. One might speculate that various mechanisms by which this could occur. For example, excitatory dopaminergic mechanisms may activate the outputs from PFC to the response systems after a particular response has been selected via the competitive interactions within PFC. Another BAS activation output can be suggested. The NAcc sends an inhibitory projection to the substantia nigra (SN). The SN provides ascending dopaminergic modulation of the caudate motor system (Gray et al., 1991). Weiner (1991) offers a clear suggestion of how NAcc output would thereby reduce dopaminergic inhibition of the caudate-putamen (CP), facilitating the execution of ongoing motor programs encoded in the cortico-striatal pathways from sensorimotor cortex to CP. In each of these BAS activation scenarios (NAcc-VP-DMNT-PFC; NAcc-VP-VTA-PFC; NAcc-SN-CP), we are suggesting that high ISS subjects would tend to produce stronger output from NAcc, with the ultimate effect of facilitating ongoing behavioral responses.

We have focused on the effects of the BAS in motivating and energizing learned motor programs. However, before moving on to consider how the BIS might modulate BAS activity within this scheme, we should briefly discuss how the BAS might affect learning processes. Two important learning processes should be distinguished: operant mechanisms which relate to the acquisition of the stimulus-response habit that comprises the motor programs; and classical conditioning mechanisms, by which a previously neutral stimulus can acquire BAS-activating properties.

As noted earlier, Houk et al. (1995) emphasized a particular form of dopamine-dependent LTP that they argued is responsible for reinforcement learning in corticostriatal pathways. We have suggested that this learning process may be the means by which neutral CSs become associated with reward and thereby are able to act as BAS input stimuli, activating NAcc neurons. In keeping with the traditional framing of RST we suggested that this learning process should be independent of the mechanisms responsible for the greater BAS reactivity of high ISS subjects. Houk et al. argue that the reinforcing properties of dopamine are mediated by D1-like receptors; we have suggested that the variations in BAS output threshold (which affect NAcc output and are the hypothesized substrate of ISS trait variation) are mediated by D2-like receptors. The extent to which D1-like and D2-like receptors are segregated from one another in the brain is a controversial topic (see Jaber et al., 1996), but our account makes it possible that in-
individual differences in the acquisition of secondary reinforcing properties by a stimulus, and individual differences in that stimulus's subsequent motivating effects, could be largely independent.

Despite the arguments just raised, it is possible that the greater VTA dopaminergic firing in high ISS subjects, in response to a BAS input stimulus, might increase the efficiency of their learning mechanisms in corticostriatal pathways relative to those of their low ISS counterparts. In addition, one might speculate that the corticostriatal learning in pathways to the NAcc might encode the acquired motivational properties of the stimulus, whereas corticostriatal learning in pathways to the caudate-putamen (dorsal striatum) might also represent some of the operant learning processes responsible for the formation of stimulus-response habits. If these speculations are correct, then both the acquisition of motivational significance for a BAS input stimulus and the acquisition of stimulus-response habits under appetitive reinforcement could be related to ISS personality traits.

The NAcc-shell also receives projections from various limbic system structures including a subcortical output from the hippocampus, plus projections from the entorhinal cortex and amygdala. These outputs to NAcc might correspond to the modulation outputs from the BIS that act to inhibit BAS activity. The amygdala output might be active in the presence of conditioned fear stimuli (LeDoux, 1996); the hippocampal output might signal an associative mismatch (when a particular stimulus is not predicted by preceding stimuli; Honey, Watt, & Good, 1998), and the output from entorhinal and adjacent cortices might signal that a stimulus is unfamiliar (Aggleton & Brown, in press). The BIS is argued to respond to each of these kinds of signal (Gray, 1982). These projections to NAcc are thought to involve the excitatory neurotransmitter glutamate; this is not a serious problem for the current proposal because there is evidence that glutamate can act to potentiate dopaminergic release and thus reduce striatal output (Imperato, Honore, & Jensen, 1990; Wang, 1991). These potential BIS modulation outputs to NAcc could therefore oppose the effects of BAS inputs (i.e., BIS modulation outputs reduce, and BAS inputs increase, NAcc output).

In the above sketch we have not proposed details for the arousal outputs from BIS or BAS, or a route by which a BIS output might directly inhibit response selection. The neurobiology of the BIS arousal output is discussed elsewhere (Gray & McNaughton, in press). Although we saw earlier that the arousal output from the BIS was critical in explaining the results obtained by Newman and his colleagues, it is possible that the other outputs omitted from Figure 10.4 may not be needed for the systems to function in the fashion described by RST. For example, the effects of an output from the BAS to an arousal system would be very difficult to distinguish from the direct behaviorally activating effects of the BAS itself. Similarly, the direct inhibitory effects of the BIS might be hard to distinguish from BIS modulation effects that act on the BAS and thereby interfere with BAS-mediated behavior. Indeed, Gray & McNaughton (in press) argue that BIS outputs affect motor systems via the subicular projection to NAcc. In the framework of the current chapter this pathway corresponds to the BIS modulation output.

HOW THE MODEL MIGHT BE TESTED

The value of the current model will, as always, be judged by its ability to stimulate research and predict experimental findings. We are currently developing a computational neural network version of the theory to aid in this process. We have begun by building a neural net based directly on striatal neurobiology (Salum, Roque de Silva, & Pickering, in press). As a complement to this bottom-up approach we have also been involved in developing a neural network, from the top down, which can simulate important learning phenomena (Schmajuk, Gray, & Lam, 1996). This model was not constrained by any particular neural architecture, but, by identifying one particular component of the model with dopaminergic neurotransmission in the VTA-NAcc pathway, we have been able to simulate specific behavioral effects of amphetamine very closely (Schmajuk, Catalin, & Gray, in press).

Modelling individual differences within networks like these will involve allowing parameters of interest (such as those reflecting dopamine receptor binding, for example) to vary and seeing whether this can capture the observed personality task correlations. To close this chapter we will describe another way in which we have begun to explore our account of ISS traits.

Those who are familiar with our account of the neuropsychology of schizophrenia (Gray et
al., 1991) will note that the neural architecture and neurochemical mechanisms proposed in that context overlap closely with the circuitry discussed here. Indeed, we related the positive psychotic symptoms (hallucinations, delusions, etc.) of schizophrenia to increases in (inhibitory, D2-like) dopaminergic effects at NAcc. As we have noted elsewhere (Gray, in press; Gray et al., in press) the link between schizophrenia and models of ISS personality traits needs careful consideration.

In this chapter, we have suggested that subjects with high scores on ISS personality traits will show increased output from NAcc neurons in response to stimuli associated with reward. We propose that this occurs because of reductions in (inhibitory, D2-like) dopaminergic effects at NAcc. The increased NAcc output is responsible for increased behavioral activation effects of reward cues in high ISS subjects and also leads to increased firing of VTA dopamine neurons that project to NAcc. Increased VTA firing might, in turn, contribute further behavioral activation effects. Based on the current model, one might therefore expect the link between schizophrenia and ISS traits to be complex.

To illustrate this, suppose one hypothesized for schizophrenics that increases in dopaminergic effects at NAcc were the result of increased VTA neuron firing (for a more plausible account see Grace, 1991). Suppose also that one had a behavioral task that was selectively influenced by VTA neuronal responses to stimulus cues. Then one might expect schizophrenic patients and subjects with high ISS trait scores to show similar behavior on such a task, and their behavior should be in the direction associated with greater VTA firing responses. By contrast, if one had another task, which was selectively influenced by the responses of GABAergic neurons in NAcc, then one might expect the behavior of high ISS subjects to reflect increased NAcc output and the behavior of schizophrenics to reflect decreased NAcc output. Despite the likely complexity of the results, we feel research that explicitly explores the relationship between ISS traits and schizophrenia will prove highly informative.

As we explain below, the relationship between ISS traits and schizophrenia may be conveniently explored by investigating the effects of ISS and schizotypal personality traits, ideally in the same sample of subjects. Healthy individuals vary in their propensities to experience mild versions of psychotic-like experiences (mild hallucinations and disorganised thinking), to hold unusual beliefs (mild delusions) and to behave in odd ways (with restricted emotions and social interactions). Many questionnaire measures have been developed to measure these aspects of schizotypal personality in healthy individuals. Several large-scale studies, using multivariate statistical techniques, have revealed a strong degree of convergence on the structure of schizotypal personality. Generally, three or four schizotypal personality factors emerge, and these factors bear a close resemblance in content to the clusters that have been found in schizophrenic symptoms (Vollema & van den Bosch, 1995).

Two schizotypal personality factors are particularly relevant for our present arguments. In all studies a major factor of positive schizotypy emerges that reflects propensities to unusual perceptual experiences and beliefs. This clearly relates closely to the positive symptoms of schizophrenia. In most studies, there is a more minor factor related to impulsive, nonconformist, and antisocial behaviors. (Vollema & van den Bosch refer to this as Nonconformity, although the impulsive component has been emphasized in the name adopted by other authors.) This factor is quite close to the kind of ISS personality trait on which this chapter has focused and indeed scales like EPQ-P load heavily on this factor. Impulsive nonconformity does not resemble any features of schizophrenia, but is similar in content to the behavior of individuals with particular kinds of personality disorder.

As argued at the start of this chapter we adhere to a continuum view of the relationship between personality traits in the healthy population and related clinical states (which are taken to reflect extremes on the personality continuum). By adopting the continuum assumption, we can use schizotypal personality variation as a means to study the processes relevant to the Gray et al. (1991) model of positive schizophrenic symptoms in healthy subjects. One can therefore compare the effects of positive schizotypy and ISS personality traits on relevant tasks and thereby more tightly constrain any model of the biological bases of these traits.

For some tasks, positive schizotypy and ISS traits appear to affect behavior in similar fashion. Negative priming is a much-studied attentional phenomenon that is reliably impaired in schizophrenics and in subjects with high scores on positive schizotypy (e.g., Peters, Pickering, & Heasley, 1994). Negative priming has also been found to be reduced by high levels of social im-
pulsivity in children (Visser, Das-Smaal, & Kwakman, 1996).

If the biological basis of ISS traits is related to striatal dopaminergic functioning, as we propose, then finding a relationship between an experimental measure of selective attention (negative priming) and impulsivity is also consistent with a role for dopaminergic neurotransmission in NAcc that encompasses more than incentive motivational processes. There is other evidence, too, for the effects of ISS personality traits on selective attention tasks (Martin, 1985). In recent work (Pickering et al., 1999) we have looked at the effect of ISS and schizotypal personality traits on a further attentional phenomenon: filtration category learning.

Filtration learning (see Kruschke, 1993) refers to a situation in which one has to classify multidimensional stimuli but only one of the dimensions on which the stimuli vary is relevant for category membership. (In our task we used visual stimuli based on a rectangular box with an internal line segment; the height of the box and the lateral position of the line segment could vary but only one of these stimulus dimensions was associated with category membership.) Thus, the subject has to learn to attend to salient stimulus features and ignore irrelevant ones. These are precisely the kind of attentional processes relevant to the Gray et al. (1991) model of schizophrenia (see also Gray et al., in press). Schizophrenics with positive symptoms would be expected to be poor at this type of learning task because the disturbance to their mesolimbic dopamine system renders them unable to learn relevance/salience normally.

In a preliminary study using only male subjects we found that subjects with high scores on Cloninger's Novelty Seeking were significantly faster at learning our filtration task than low scoring subjects. In a subsequent study we measured positive schizotypy using Mason, Claridge, and Jackson's (1995) Unusual Experiences scale and ISS personality via EPQ-P. Based on the first study a positive correlation between learning and EPQ-P scores was expected. For the whole sample there was only a nonsignificant trend (r = .22, p = .065), but the correlation did reach significance in the male subjects (r=.35). In the same subjects, the correlation between learning and Unusual Experiences scores was negative as predicted, although nonsignificant. However, the correlation was significant in female subjects (r = -.38, p < .05). Taken together with the negative priming findings, the filtration learning results suggest that schizotypal and ISS personality traits may sometimes have opposing, and sometimes similar, effects on behavior. This was exactly the kind of complex relationship that we anticipated above.

For the moment, these data serve to show that there is plenty of work to be done in order to disentangle the complex relationships between schizotypal and ISS personality traits. Such findings, if they prove reliable, will present a considerable challenge to our attempts to model personality traits via biologically constrained neural networks.

The effects of ISS traits on filtration category learning extend earlier findings by Ball and Zuckerman (1990), who showed that subjects with high scores on the Sensation Seeking scale (Zuckerman, 1979) learned a complex concept formation task faster than subjects with low Sensation Seeking scores. The concept formation task, like our filtration paradigm, involved distinguishing relevant from irrelevant stimulus attributes, and the personality effect was found whether or not successful performance was rewarded with money. Finally, in light of the relationship between ISS traits and Parkinson's disease, reviewed earlier, it is interesting to note the findings of Knowlton, Mangels, and Squire (1996). Knowlton et al. found that Parkinson's disease patients showed poor category learning (forecasting the weather by learning the associations with probabilistic visual geometric cues presented on a computer screen), despite having normal episodic memory for details of the category task (e.g., screen layout etc.). Once again, this task involved learning which stimulus attributes were relevant in predicting outcome.

This set of experimental outcomes may once again illustrate that the influence of the dopaminergic substrate of ISS personality traits can be seen in behavioral contexts other than those controlled by explicit appetitive incentives. This is in keeping with our view that the mesolimbic dopamine system responds to a wider range of stimuli than those which transmit appetitive incentive information.

CONCLUDING OBSERVATIONS

We presented the model developed in this chapter to show that it is now possible to use an integrated neuroscience approach to the study of personality. We hope that this kind of approach will improve the status of personality research in
the eyes of the psychology and neuroscience communities. We feel that, by drawing together data from a wide range of research areas, we have been able to sketch a reasonably specific, and we hope persuasive, account of the neuroscience of ISS personality traits. This type of personality theory can also be tested by the usual methods of natural science.

We chose to focus on ISS traits in part because there is a degree of consensus in this area among the major biologically oriented personality theorists, and our model resembles other proposals, especially the recent account of Depue and Collins (in press). Depue and Collins argue that there is a dopaminergic substrate to Extraversion that is weakly and inconsistently related to correlations between ISS traits and dopamine-sensitive measures. In our version, by contrast, it is ISS traits themselves that are closely aligned with the fundamental biological axis of personality, and Extraversion that correlates with dopamine-sensitive measures by proxy.

The current model relates ISS traits to variations in dopaminergic transmission in the mesolimbic pathways from VTA to NAcc and suggests that NAcc is a vital part of a behavioral activation system (BAS) concerned with appetitive motivational effects on behavior. However, we have repeatedly emphasized that one should not align dopaminergic release in NAcc exclusively with appetitive motivation. In the current model, other kinds of signal, reflecting other ways in which a particular stimulus might be salient (because it is unfamiliar, unpredicted by preceding stimuli, or because it signals an upcoming aversive event), also have the capability to stimulate dopamine release in NAcc. We view these other signals as being generated in one of a number of neural loci. We describe these other loci collectively as forming a Behavioral Inhibition System (BIS) that functions to inhibit ongoing behavior, in part through opposing the effects of the BAS. Elsewhere we have related individual differences in the strength of the output signals from the BIS to variations in trait anxiety (Gray & McNaughton, 1996, in press).

REFERENCES


Chapter 10. The Neuroscience of Personality


Gray, J. A. (in press). But the schizophrenia connection... Behavioral and Brain Sciences.


