Psychopharmacology of moral and social judgments

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With sincere respectful gratitude

This thesis is dedicated to Professor Phil Cowen

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Chapter 3:

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ABSTRACT

This thesis is an interdisciplinary project in experimental social psychology, psychopharmacology, neuroscience, and neuroethics. The role of emotion in higher order psychological processes – social and moral judgments – was investigated. Specifically the role of noradrenergic mediated emotional arousal was researched. Behavioural studies demonstrated that acute beta adrenergic blockade with propranolol led to a reduction in negative implicit racial associations and also a modification of moral decision making. These findings suggest that basic affective processes might be causally relevant for higher order evaluations. However, enhancement with the noradrenergic potentiating agent reboxetine did not show effects opposite to those of propranolol on racial attitudes or moral judgments, which might indicate that emotional arousal, specific to beta-adrenoceptors might be involved in the effects of propranolol. Further a pharmacological fMRI study demonstrated that the activation pattern in brain regions commonly associated with intergroup bias -- such as the amygdala, insula, dorsolateral prefrontal cortex, and fusiform gyrus -- was affected by propranolol, and that the effect in the amygdala was correlated with implicit racial bias.

Taken together the research suggests that automatic emotional arousal plays a role in higher order psychological processes, such as moral and social judgments, which aids the understanding of the underlying neurobiology of such processes. Finally, the ethical implications – such as the prospect of pharmacological moral enhancement – are discussed. The findings also suggest that the moral and social effects of already widely used psychotropic medications should be subject to further empirical and ethical investigation.

DETAILED ABSTRACT

This thesis examines the role of noradrenaline in moral and social judgements. It first reviews the literature on moral psychology and explores the recent debate about the involvement of emotional and rational factors in moral judgments. Dating back to ancient philosophy, the question of the predominant role of reasoning versus emotion in morality has been examined. One of the current theories, influenced by neuroscience research, suggests that intuitive judgments can be distinguished from moral decisions that are based on deliberate reasoning, and that both reactions might conflict. Thus influencing specific emotions might affect individuals' judgments of right or wrong. Secondly, the thesis reviews the social psychology literature on intergroup bias and again explores the evidence for the theory that emotional arousal might be relevant for some forms of racial prejudice. Specifically it has been suggested that basic emotional arousal, such as fear responses, might play a central role in implicit, "unconscious", forms of attitudes to other races, whilst cognitive aspects might have a stronger influence in overt forms of stereotypical knowledge and explicit prejudice. Building on the results of previous work and subsequent theory, this thesis addresses the role of emotion in moral and social judgments, delivering further evidence for current theorising of the predominant role of emotional arousal in higher order social concepts. Specifically, the aim was to explore if emotion was indeed *causally relevant* for both moral judgments, and implicit racial associations.

The first chapter also introduces the method of using psychopharmacology, and pharmacological fMRI, as a research tool to address the hypothesis. The literature on noradrenaline and how this transmitter is involved in emotional processes is then reviewed. Specifically, research that has demonstrated an effect on emotion processing after beta-adrenergic blockade is examined. In sum, the first chapter gives an overview of the current open debate on emotion and cognition being involved in moral and social judgments, and it

demonstrates that the method of using beta-adrenergic blockade in combination with fMRI might help to gain further insights into the question of the causal relevance of emotion in moral judgments and racial prejudice.

Chapter 2 then presents Study 1 which investigated the role of noradrenergic transmission in moral decision-making. This experiment studied the effects in 40 healthy volunteers of propranolol (a noradrenergic beta-adrenoceptor antagonist) on moral judgment in a set of theoretical moral dilemmas, involving decisions such as killing one to save a greater number of individuals, in a double-blind, placebo-controlled, randomised group design. Propranolol (40 mg orally) significantly reduced heart rate, but had no effect on self-reported mood. Importantly, propranolol made subjects more likely to judge harmful actions as morally unacceptable, but only in dilemmas where harm depicted was 'up close and personal' (i.e., active, direct harm). In addition, longer response times for such personal dilemmas were only found for the placebo group. Finally, judgments in personal dilemmas by the propranolol group were more decisive. These findings indicate that noradrenergic pathways play a role in responses to moral dilemmas, in line with recent work implicating emotion in moral decision-making. However, contrary to current theorizing, these findings also suggest that aversion to harming is not driven by emotional arousal.

Chapter 3 presents research on the effect of noradrenaline on implicit attitudes (Study 2). In this study healthy volunteers (N = 36, a subsample of Study 1/Chapter 2) of white ethnic origin, received a single oral dose of propranolol (40 mg). Subjects completed an explicit measure of prejudice and the racial implicit association test (IAT), 1-2 hours after propranolol administration. Importantly, relative to placebo, propranolol eradicated implicit racial bias, without affecting the explicit measure of prejudice. These results indicate that β-adrenoceptors play a role in the expression of implicit racial associations,

suggesting that noradrenaline-related emotional mechanisms may mediate negative racial bias.

Chapter 4 reports research on the role of noradrenergic transmission enhancement on moral decisions and intergroup attitudes (Study 3 and Study 4). The aim was to further explore the possibility that enhanced emotional arousal might lead to more utilitarian decisions (via reduced harm aversion) and increased negative implicit racial associations. In a double-blind placebo-controlled randomised study 40 subjects received either placebo or a single dose of reboxetine (4 mg). Reboxetine, an antidepressant medication, is a noradrenaline reuptake inhibitor, with multiple effects on emotional processing that also vary during the course of treatment. Previous research has demonstrated that reboxetine increased processing of positive stimuli in healthy volunteers, but it also might increase negative emotional responses during short term interventions. In the present study, reboxetine significantly enhanced heart rate at its peak concentration time of 2 hours. Contrary to predictions, however, reboxetine did not have a significant effect on responses to any of the theoretical moral dilemmas. In addition, this study included additional moral dilemmas involving less harmful acts, such as lying. Here reboxetine led to a slight, but non-significant, increase in utilitarian judgments. In addition, reboxetine did not affect explicit or implicit racial attitudes. There was a trend for reboxetine to enhance response times to incongruent racial categorisations, but it did not increase the speed on congruent trials. It is suggested that moral judgments and implicit racial associations might be underpinned by specific emotions that were selectively targeted by noradrenaline reduction through beta adrenoceptors; however, global enhancement of noradrenaline through both alpha and beta adrenoceptors did not have opposite enhancing effects.

Chapter 5 reports an fMRI study (Study 5). This study was conducted to identify underlying central neural correlates of the effect of propranolol on implicit racial

associations. Thirty subjects received propranolol or placebo in a double-blind, randomised manner. Subjects viewed unfamiliar black or white faces during the scan and subsequently completed the IAT. Propranolol led to reduced activity for black compared to white faces in amygdala, fusiform gyrus, insula, and dorsolateral prefrontal cortex. In addition, amygdala activity correlated with the IAT score, which was lowered by propranolol. This study supports the theory that automatic emotional arousal, such as fear responses, is *causally* involved in implicit racial bias, and demonstrates that drug intervention might modify negative racial associations through action in the amygdala.

Even though this thesis was mainly based in experimental psychology it has been an interdisciplinary project (psychology, neuroscience, and philosophy) that has also led to numerous ethical questions regarding pharmacological moral enhancement. For example, the study of propranolol and racial prejudice has received extensive media coverage, also addressing numerous ethical questions mainly regarding the possibility of pharmacological moral human enhancement. Thus Chapter 6 explores the neuroethics of moral enhancement using noradrenergic or other pharmaceuticals and explores the philosophical and policy implications of this and other research on this topic. The prospect of the development of pharmaceuticals specifically designed to enhance normal cognitive, affective and motivational processes has interested and concerned many people. This chapter first reviews evidence for moral effects of pharmaceuticals currently already widely used for medical treatments. It will be argued that the moral effects of these and other widely-used pharmaceuticals warrant further empirical research and ethical analysis. Finally, Chapter 7 discusses the implications of the research for psychological and neuroscience theories of racial attitudes and moral judgements. The reported research gives further evidence for the role of automatic emotional arousal in implicit but not explicit racial attitudes. Importantly, the results of the pharmacological fMRI study suggest that

neural circuits influenced by noradrenaline, and specifically the amygdala, might indeed be causally relevant for emotional automatic evaluations of social stimuli. Further research may explore if the effect would persist in the course of intervention and also if long term implicit attitude changes might lead to behavioural and also explicit prejudice changes. Additionally, this chapter discusses the finding that noradrenergic mediated arousal led to increased deontological moral judgments. Again, the view that emotion plays a predominant role in moral judgements was supported. However, contrary to current theorising, the involvement of emotion might be more complex than previously theorised. Further it will be discussed how future research might advance assessment methodology for moral judgments.

In conclusion, it has been shown in this thesis that basic automatic emotional arousal is involved in, and also causally relevant for, higher order judgments and that it might indeed be possible to change attitudes and morality by manipulating basic neurochemistry. This leads to considerable ethical questions regarding the social and moral effects of pharmaceuticals already widely used and also in terms of the prospect of moral enhancement for society.

CHAPTER 1: GENERAL INTRODUCTION:

NORADRENALINE, AND SOCIAL, AND MORAL JUDGMENTS

"The lower levels in the neural edifice of reason are the same ones that regulate the processing of emotions and feelings, along with the body functions necessary for an organism's survival. In turn, these lower levels maintain direct and mutual relationships with virtually every bodily organ, thus placing the body directly within the chain of operations that generate the highest reaches of reasoning, decision making, and, by extension, social behaviour and creativity. Emotion, feeling and biological regulation all play a role in human reason."(Damasio, 1994, p. xvii).

Indeed, emotions (i.e., affectively valued states, Ortony, Clore, & Collins, 1988), such as fear, anger, happiness, sadness, surprise, and disgust might affect higher order, and seemingly rational judgments and attitudes. Numerous theories in social and moral psychology have discussed the involvement of emotion in moral and social judgments (e.g., Cushman, Young, & Greene 2010; Huebner, Dwyer, & Hauser, 2009; Levy, 2007). However, emotions might have a more substantial and also causal effect on higher order processes, processes such as moral decisions and racial attitudes. First I will separately review the literature on moral and social psychology that has explored the role of emotion in racial attitudes and moral judgments. Then I will focus on the open questions in this current debate and discuss the use of psychopharmacological methods to study the causal role of emotion in higher order judgments. I will then review the evidence for noradrenaline being involved in emotional arousal and basic emotional processes and how beta-adrenergic blockade could be used to research the effect of primary emotional arousal in intergroup prejudice and moral decision making.

Introduction to moral philosophy and psychology

Moral decision making has hitherto been largely a matter of philosophical investigation, but more recently has been considered from both a psychological and neuroscience perspective. The earliest investigations of morality can be found in Plato's

writings over 2000 years ago (Casebeer & Churchland, 2003). Despite this long history, even an agreed definition of morality has proven to be problematic. Wallace and Walker (1970) published a book solely on the topic "Definition of Morality", with the conclusion that they could not find a suitable consensual definition. Casebeer and Churchland (2003) defined moral reasoning as "… a series of acts that result in a conclusion about what one ought to do or think" (p. 16). Additionally, moral transgressions (e.g., killing someone) have been distinguished from conventional transgressions (e.g., eating without cutlery) (Turiel, 1979). In a series of experiments, Turiel (1979, 1983) found that individuals differentiate between moral and conventional transgressions on a number of factors, such as authority dependence, universality, content, and seriousness (i.e., moral transgressions are seen as having prescriptive force, proscribed over different situations, and involving serious injustice or harm of another person).

A number of different philosophical approaches to morality can be distinguished. According to the cognitive approach, rational reasoning plays a crucial role in moral decision making (e.g., Kohlberg, 1969). Moral cognitivism implies that moral statements can be either true or false. It is proposed that rational knowledge of moral rules and other essential intellectual skills (i.e., perspective taking) are acquired during development. Kohlberg's theory of moral development (1969) suggests different stages of moral reasoning, starting from young children who determine right and wrong according to reward and punishment, to adolescents who are able to find abstract reasons for existing moral rules. Opposite to these cognitive approaches are emotivists, emphasising the major role of emotion in morality (e.g., Hume, 1960). According to emotivists, moral statements are declarations of preference. Sentimentalism also supports the idea that emotion plays a central, causal role in moral judgments (Nichols, 2008). For example Gibbard (1990) argued that feeling guilty about an action is the central emotional response guiding moral

choice. Furthermore, a distinction can be made between intuitionism versus rationalism (e.g., Shweder & Haidt, 1993). Intuitionists believe that moral appraisals are generated rapidly/ automatically, while rationalists argue that moral truth can be acquired through a process of argumentation and deductive reasoning (e.g., the philosopher Immanuel Kant). Besides emotivists, intuitionists also believe that emotion plays an important role in morality (Shweder & Haidt, 1993). It is thought that emotional responses involve automatic cognitive appraisals (Lazarus, 1991). Shweder and Haidt (1993) have argued that these automatic cognitive appraisals are similar to the self-evident truth of morality (i.e., that there is a moral truth but it is not acquired through conventional knowledge). For example, anger that is experienced as a result of injustice or personal assault, can be counted as being self-evident truth of morality. Besides these long established directions from thinkers in philosophy, recent influential theories about moral judgements have also been recognized in moral psychology. These theories mostly emphasise the predominant role of emotion in moral judgments.

Haidt's theory of moral decision making

Haidt (2001) suggested that moral decisions are the product of quick and automatic intuitions, which are acquired early in development, predisposed by evolutionary disposition. Conscious reasoning on the other hand occurs after a moral judgement is made, as a post-hoc justification of an already preferred option chosen by intuition. The reasoning process is therefore biased towards the initial evaluation. Haidt (2003) suggests that only on some rare occasions, for example if intuitions are in conflict, is conscious reasoning applied during the initial decision process. Haidt (2003) argued that emotions are a crucial part of intuitions and suggested that sentiments give an immediate feeling of what is right and wrong. In a series of behavioural experiments involving theoretical moral dilemmas Haidt and colleagues found that individuals were often unable to deliver

sufficient justifications for their moral choices, supporting the role of intuition in moral decisions (e.g., Haidt & Bjorklund, 2008).

Neuroscience approaches to morality

Neuroscience theories (e.g., Greene, Nystrom, Engell, Darley, & Cohen, 2004; Greene, Sommerville, Nystrom, Darley, & Cohen, 2001;), and neuropsychological investigations of decision making in general (e.g., Damasio, 1994) mainly support combined models of moral judgements and decision making. Within his influential studies on patients with ventromedial prefrontal cortex damage, Damasio (1994) first introduced the important influence of emotion in general decision making. Bechara, Damasio, Tranel, and Damasio, (2005) showed that healthy subjects developed anticipatory skin conductance responses to disadvantageous decisions, helping them to choose the better option. Importantly, the somatic/ emotional response towards disadvantageous choices proceeded the explicit knowledge, demonstrating that emotional bodily reactions facilitated the decision making process. Regarding moral decision making, Greene et al. (2004) suggested that emotional and cognitive processes compete, leading to conflict. Furthermore, Greene et al. (2001) suggested that deontological moral judgments (e.g., judgments that determine the moral worth of an act, regardless of its consequences) are driven by emotion, whilst utilitarian judgments (i.e., where judgments of morality are determined by calculation of the resulting outcome) are caused by cognitive processes overriding initial emotional choice. In their studies Greene et al. (2001, and 2004) used hypothetical moral dilemmas; famous examples of these are the footbridge and the trolley dilemmas (Thomson, 1971) (See also Figure 1.1);

Trolley dilemma "You are at the wheel of a runaway trolley quickly approaching a fork in the tracks. On the tracks extending to the left is a group of five railway workmen. On the

tracks extending to the right is a single railway workman. If you do nothing, the trolley will proceed to the left, causing the deaths of the five workmen. The only way to avoid the deaths of these workmen is to hit a switch on your dashboard that will cause the trolley to proceed to the right, causing the death of the single workman. How morally acceptable is it to hit the switch in order to avoid the deaths of the five workmen?" (p. 104).

Footbridge dilemma "A runaway trolley is heading down the tracks toward five workmen who will be killed if the trolley proceeds on its present course. You are on a footbridge over the tracks, in between the approaching trolley and the five workmen. Next to you on this footbridge is a stranger who happens to be very large. The only way to save the lives of the five workmen is to push this stranger off the bridge and onto the tracks below where his large body will stop the trolley. The stranger will die if you do this, but the five workmen will be saved. How morally acceptable is it to push the stranger on to the tracks in order to save the five workmen?" (p. 105).

Figure 1.1. Decision in hypothetical moral dilemmas.

Figure 1.1. Decision in hypothetical moral dilemmas. Famous thought experiments in moral philosophy. Examples are the footbridge and the trolley dilemma. The picture shows 5 versus 1 railway workmen. Photograph taken by the author, in Reading, on the Oxford-London railway track; September, 2012, 12.15 a.m.

Usually, individuals make more deontological decisions (regard the action as morally unacceptable) in the footbridge dilemma than the trolley dilemma, even though the outcome for both dilemmas is objectively the same. In his fMRI study Greene et al. (2001) presented subjects with these and other moral dilemmas during the fMRI scan. The researchers classified some theoretical dilemmas as personal and some as impersonal. Criteria for personal (or "up close personal") dilemmas were that: a) serious bodily harm was caused to b) a person in a way that c) did not simply reflect redirecting pre-existing harm onto another person (indicating agency). For example the trolley dilemma was rated as impersonal, and the footbridge dilemma as personal. Greene et al. (2001) found that activation in brain regions previously suggested to be involved in emotion, such as the amygdala, medial frontal gyrus, and the posterior cingulate was associated with personal dilemmas. Impersonal dilemmas on the contrary activated brain regions associated with reasoning and working memory. Additionally, utilitarian judgments in personal dilemmas were associated with longer response times and neuronal activity in brain areas associated with cognitive control (anterior dorsolateral prefrontal cortex, anterior cingulate). In accordance with their findings Greene (2001, 2003, & 2008) proposed the involvement of automatic emotional responses in moral decision making. The authors particularly hypothesized that deliberate reasoning might conflict with emotional responses in some instances. For example, to form a utilitarian judgment in a personal dilemma, individuals would have to override their emotional response that would lead them to a deontological decision (i.e., intentionally killing is wrong). Thus Greene et al. (2001, 2004, & 2008) suggested that deontological judgments were driven by emotion and that utilitarian judgments were driven by cognitive control. The method and design of this fMRI study, as well as the theoretical conclusions, have however been criticized (Kahane & Shackel, 2010; Moore, Clark, Kane, 2008). Most important is the fact that the categories of

impersonal and personal dilemmas involved further dilemmas that were very different from each other, possibly on a large number of other dimensions. For example, in the category of personal dilemmas the authors also used the `crying baby` dilemma compared to using the `lost wallet` dilemma for the impersonal category. Here a dilemma that described the act of smothering one's own baby was contrasted to the question of the moral acceptability of keeping money found in a lost wallet. Further, neuroscience research on moral judgments in general has also been criticised by philosophers Casebeer and Churchland (2003). The authors argued that neuroscience experiments often lack ecological validity (see also Chapter 7 for a discussion). The authors criticised that an assessment of moral decision making might be difficult since a precise definition of morality, which is important for successful neuroscience investigations, is already difficult to establish. However, the idea that emotions are involved in moral decision making has also been supported by lesion research (e.g., Barrash, Tranel, & Anderson, 2000; Moll, de Oliveira-Souza, Bramati, & Grafman, 2002). Damage to the ventromedial prefrontal cortex (VMPC) (a brain area strongly associated with emotion and cognition integration; Young & Koenigs, 2007) impairs not only the integration of emotional responses into decision making in general but also moral functioning. For example, affected individuals show a number of abnormalities such as grossly antisocial behaviour, a tendency to make mostly utilitarian judgments in moral dilemmas, and an immature moral development (Barrash et al., 2000; Moll et al., 2002; Young & Koenigs, 2007). In addition, VMPC activity has also been observed in fMRI studies comparing passive viewing of moral as opposed to non-moral pictures (e.g., a car accident was described as an unreal TV event, or as happening for real and being reported in the news; Harenski & Hamaan, 2006) showing the likely importance of this brain region to moral evaluations. Besides neuroscience research, evidence for the involvement of different emotions in morality can also be found in

psychological behavioural experiments. Indeed research has demonstrated that basic emotions as well as secondary emotions impact decision making in general and moral decision making and moral behaviour in particular.

Basic emotions in moral judgments[1]

It has been demonstrated that basic emotions can have an effect on reasoning (Pham, 2007), including working memory capacity (i.e., Darke, 1988), categorisation of stimuli (Isen, Niedenthal, & Cantor, 1992), problem-solving (Isen, Daubman, & Nowicki, 1987), self-control (Fry, 1975) and risk taking behaviour (Johnson & Tversky, 1983). Pham (2004) suggested that emotions were often used as informational sources for ascribing value (i.e. things that feel good must be good). But basic emotions might also influence decisions about moral issues. Carlson and Miller (1987) for example, found that positive mood enhanced pro-social behaviour. And Scher (1997) demonstrated that anger and sadness were linked to higher perceptions of injustice and immorality. Trafimow, Bromgrad, Finlay, and Ketelaar, (2005) found that individuals were more utilitarian in moral decisions if they misattributed their emotional arousal to an external source rather than to the moral situation. In addition Wheatley and Haidt (2005) found that subjects, who were hypnotized to feel disgust while hearing a certain word made more severe moral judgments in situations that involved this word than subjects who were not hypnotised in such manner.

Secondary emotions in morality

Secondary emotions, particularly moral emotions, differ from primary emotions in that they are often linked to the welfare of society or an individual (Haidt, 2003). Moll

[1] I understand that the distiction between basic emotions (fear, anger, sadness, happiness, surprise, disgust) (Ekman et al., 1982) and secondary emotions (e.g., shame, guilt, contempt) has sometimes been questioned (e.g., Ortony & Turner, 1990). However I will keep this generally accepted distinction as a working definition.

(2008) suggested that moral emotions typically include guilt, pity, embarrassment, shame, pride, awe, contempt, indignation, and gratitude. It has been argued that moral emotions might be elicited in response to violations of social norms and stereotypes that code for individual attitudes and beliefs (Nichols, 2002). In his review, Pham (2007) concluded that secondary emotions have a function in promoting socially and morally desirable behaviour. Further, Eisenberg (2000) suggested that moral emotions play a crucial role in helping people to evaluate moral features, motivate moral behaviour, and suppress immoral acts. Pham (2007) argued that anticipation of negative emotions, such as guilt, would prevent individuals from norm violating behaviour. Anticipated emotions, such as anticipated regret or shame, have been demonstrated to influence choice behaviour in decisions (Mellers, Schwarz, & Cooke 1998). Recently, in one of the first psychopharmacological studies in moral psychology, Crockett, Clark, Hauser, and Robbins (2010) found that administering a selective serotonin reuptake inhibitor (SSRI) (Citalopram) led to an increase in deontological moral judgments. The authors used hypothetical moral dilemmas based on Greene et al. (2001). In a double blind placebo controlled study, the authors found that SSRI intervention increased deontological judgments in personal but not in impersonal moral dilemmas. Crockett et al. (2010) argued that increased serotonin levels might have led to an increase in harm aversion, supporting the role of serotonin in association with pro-social emotionality.

Interaction of cognitive and emotional factors

Aristotle argued that "… sensibility, desire, and judgement all have roles in which they are aligned in the well-ordered agent. Neither reason alone nor is sensibility adequate to explain morally relevant human action." (Jacobs, 2006, p. 245). However, the extent and causal relevance of emotion and reason in morality has forcefully been debated (e.g., Cushman, Young, & Greene, 2010; Huebner, Dweyer, & Hauser, 2008; Levy, 2007). For

example, Joyce (2008) argued that simply because emotional activation is found during moral decision making using neuroscience methods, it does not necessarily follow that emotion is the only expression of moral judgements. Huebner et al. (2008) argued that current neuroscientific and other evidence does not sufficiently support the claim that emotion *is necessary* for moral judgments. Nichols and Mallon (2005) for example demonstrated that in unemotional "personal" dilemmas (e.g., throwing a teacup from a bridge to save five other cups) the utilitarian bias for the "teacup-footbridge" dilemma as opposed to the "teacup trolley dilemma" was present, suggesting that there is reasoning rather than an emotional explanation for the observed asymmetry.

Levy (2007) considers that affective components might cause or reinforce the corresponding belief, suggesting that the factors complement each other. Levy also suggested that moral beliefs and moral intuitions might contradict one another. This is in accordance with Greene et al. (2001), who also argued that sometimes emotional and cognitive responses might be in conflict with each other. A multi-system approach for moral judgments was introduced by Cushman et al. (2010). The authors suggested that most successful approaches in moral psychology usually disregard the emotion/cognition debate and focus on multiple system ideas. Cushman et al. (2010) argue that moral judgments rather consist of intuitive and rational processes equally. Whilst the cognitive system operates "controlled" reasoning, affective processes are generated automatically/ unconsciously, an approach in line with Greene et al. (2001, 2004), suggesting differential processing streams for emotion and cognition. However, Greene et al. (2001) also found that emotion and cognition were differentially activated depending on the moral dilemma (e.g., up-close personal versus impersonal). This might indicate that for some moral decisions (i.e., those high in eliciting emotional arousal) conflict between emotional and cognitive processes might arise. In addition, in an fMRI study Borg, Hynes, Van Horn,

Grafton, and Sinnott-Armstrong (2006) found moral scenarios involving intentional rather than unintentional harm elicited greater activity in brain areas commonly associated with emotional processing. Moral statements involving unintentional harm engaged areas associated with cognition.

The debate on the role of emotion and cognition is moral judgments is still ongoing. Most importantly, the claim that emotion is necessary – and causally relevant – in the formation of moral decisions has not yet been fully explored and demonstrated (Hueber et al., 2008; Joyce, 2008; Nichols, 2005). Later in this chapter I will discuss how noradrengergic manipulation of emotional arousal might help to increase knowledge about the question of the causal involvement of basic emotions in morality. But first I will turn to reviewing a different area of higher order cognition - that of intergroup attitudes and social judgments - and draw similar attention to the on-going debate about the role of emotion in social evaluations.

Emotional factors in social judgments[2]

Research on prejudice and stereotypes goes back to the 1920s and 1930s, a time when there was overt racial conflict in the United States between the white majority and the black minority. German anti-Semitism also contributed to research into prejudice and stereotypes. The social relevance of prejudice was demonstrated by Allport (1954) in his classic book, "The Nature of Prejudice". However, in the post-World War II area social norms began to shift, accompanied by a declining expression of overt racial prejudice (Schuman, Steeh, Bobo, & Krysan, 1997). Importantly, however, race-biased reactions continue to be found in contemporary society, especially on measures of implicit attitudes,

[2] Note that the term "out-group" refers to the group the individual does not below to (i.e., in-group versus out-group).

which are beyond conscious control and intention (Greenwald, McGhee, & Schwartz, 1998).

There has been considerable debate about precise definitions of prejudice and stereotype (for a discussion see for example Zanna & Rempel, 1988). Whereas prejudice is a (typically negative) attitude towards an out-group and/or its members, a stereotype can be defined as a consensual belief about the characteristics of a social category (Hewstone, Rubin, & Willis, 2002). As a consequence of social categorization, individual characteristics are overlooked. Zanna and Rempel (1988) suggested that an attitude, an overall evaluation of a person or object, is based on affective (e.g., feelings about the attitude object), cognitive (e.g. beliefs about the attitude object), and behavioral (e.g., information regarding past behavior intentions towards the attitude object) components. According to Allport (1954) prejudice can be defined as a "feeling, favourable or unfavourable, toward a person or thing, prior to, not based on actual experience." (Allport, 1954, p. 6). Prejudicial evaluations of other individuals might for example be based on their race, religion, or disability. Other than explicit thoughts and stereotypes about out-group members, individuals form implicit associations towards out-group members that might be automatic and occur even with a sincere explicit believe in equality (Nosek, Hawkins, & Frazier, 2011). Indeed the association between explicit and implicit out-group evaluations is typically weak (~ $r < .15$) (Nosek, Greenwald, & Banaji, 2007), which suggest that both might have distinct underlying psychological mechanisms (Nosek et al, 2011).

The implicit association test (IAT) (Greenwald et al., 1998) is a widely used method to assess implicit attitudes to which individuals may have limited introspective access (Nosek et al., 2007). In this item-sorting task, latency differences between "prejudice" congruent and incongruent trials are evaluated, to measure implicit bias. There

is now extensive evidence that the IAT is a reliable measure of implicit attitudes towards social out-groups, whether based on race, sexual orientation, gender, or political preference (Nosek et al., 2007) (See chapter 3 for more details on the IAT). A recent meta–analysis further suggests that the IAT is a consistently better predictor of some forms of discrimination against out-group members than are measures of explicit prejudice (Poehlman, Uhlmann, Greenwald, & Banaji, 2004). It has been suggested that implicit measures best predict subtle and spontaneous biased behaviour (Nosek et al., 2007), whereas explicit prejudice measures more reliably predict deliberate behaviour, such as overt discrimination (Fazio, Jackson, Dunton, & Williams, 1995). Several specifically neuroscience, studies have suggested that, compared to explicit prejudice, implicit prejudice involves a stronger emotional component (Lieberman et al., 2005; Wheeler & Fiske, 2005).

Neuroscience of prejudice

One of the first brain imaging investigations, showing inter-race biases, was conducted by Phelps et al. (2000). The authors used fMRI to assess the blood-oxygen-level-dependent (BOLD) responses in association with white, compared to black, unfamiliar male faces (subjects were white Americans). Additionally, they assessed race-related attitudes of the subjects using implicit and explicit measures. Importantly, the authors found that the magnitude of the BOLD response was significantly correlated with the implicit (but not the explicit) measure of race prejudice. These initial findings were supported in further research (Cunningham, Johnson, Raye, Gatenby, Gore, & Banaji, 2004), which also indicated that, generally, other-race faces were associated with increased amygdala activation, and that the inter-race bias was even found to be more profound when faces were presented subliminally (Cunningham et al., 2004). This suggests that automatic emotional arousal might play a key role in implicit but not explicit attitudes.

However, contrary to this Phelps, Cannistraci, & Cunningham, (2003) found that a patient with bilateral lesion to the amygdala still demonstrated a reliable IAT effect. Further research has demonstrated that structures with reciprocal connections to the amygdala, including the dorsolateral prefrontal cortex (dlPFC) and the anterior cingulate cortex (ACC) might contribute to higher-order controlling mechanisms of the initial evaluation of outgroups (Cunningham et al., 2004; Knutson, Mah, Manly, & Grafman, 2007; Richeson et al., 2003; Stanley, Phelps, & Banaji, 2008). Within their neural model of implicit and explicit attitudes, Standley et al. (2008) proposed that ACC activation might reflect the conflict between the implicit reaction and propositional explicit cognitions. These brain activation patterns, associated with out-group perception, may however not be inevitable and are task and context dependent. Using fMRI, Wheeler and Fiske (2005) showed that the rapid amygdala response was dependent on the perceiver's current social-cognitive goal (i.e., group categorization versus mere inspection). In addition Golby, Gabrieli, Chiao, & Eberhardt, (2001) demonstrated that racial bias in the fusiform face area could be modulated by intergroup contact. This might also explain the findings of Phelps et al. (2000), who demonstrated amygdala and IAT correlations only if out-group faces where unfamiliar, rather than familiar.

fMRI studies are, however, always correlational and cannot establish a causal link between brain activation, or indeed automatic emotional arousal and implicit racial associations. In the following I will demonstrate how pharmacological fMRI might aid the understanding of emotional arousal being causally involved in implicit attitudes.

Open questions and psychopharmacology as a research method

As demonstrated in the previous two sections, for both moral and social judgments it was suggested that emotions may indeed play an important causal role. Some strong evidence for this comes from fMRI research that, as stated before, is correlational and cannot establish a causal link. Thus for example Hueber et al. (2008), Joyce (2008), and Nichols (2005) proposed that the role of emotion in morality could to date not fully be determined. In addition, conflicting evidence was found. For example, even though amygdala activity correlated with the IAT score (Phelps et al., 2000), an intact IAT was found in one patient with bilateral amygdala damage (Phelps et al., 2003). And in moral psychology, as stated before, even though activation in emotion related areas was found for personal compared to impersonal moral dilemmas (Greene et al., 2001), the behavioural distinction between personal and impersonal moral dilemmas still existed if the emotional content was taken out of the moral dilemmas (e.g., teacups instead of people).

Using psychopharmacology, a new method might contribute new insights to the debate, and deliver a research method that might allow establishing a causal link between emotion and a psychological concept, such as prejudice or moral judgments. In psychopharmacological studies drug versus placebo intervention is utilised in a double blind randomised manner. The drug that manipulates the function of specific brain neurotransmitters is then used as a tool to investigate if these neurotransmitters are indeed causally relevant for the psychological concept. For example, serotonin is thought to increase prosocial behaviour and, as noted above, Crockett et al. (2010) found that increasing serotonin function did impact on certain forms of moral judgements.

One possible approach to determine the role of emotion in moral and social judgments is to employ a drug that is thought to diminish basic emotional arousal. If this

then leads to changes in the performance of tasks tapping moral and prejudicial behaviour, then further insights might be gathered about the role of emotional mechanisms in these processes. In the following section, a brief introduction to affective neuroscience and psychopharmacology will be given. I will then outline the extensive evidence for the role of noradrenaline and sympathetic activation in basic emotional arousal. Finally, I will suggest that beta adrenergic blockade via propranolol could be associated with a reduction in basic automatic emotional arousal, and identify how this then might help to determine the role of basic emotions in moral and social judgments.

History of affective Neuroscience

James, (1884) ground breaking but controversial theory (Cannon, 1927) proposed that emotions are the experience of bodily changes which occur automatically following stimulus presentation. The famous example is that of individuals who are not running away from a bear because they feel frightened, but who, because they are automatically running away after the bear encountered, then feel frightened. James (1884) proposed that different bodily changes would code different emotions. Indeed very early research has already demonstrated that fearful stimuli elicit the so called "fight and flight" response in animals and humans, a response which is caused by sympathetic nervous system activation (Weiss, 1971), and which is indicative of adrenaline and noradrenaline release (Ax, 1953).

Introduction to basic psychopharmacology

Nerve cells conduct bioelectrical signals to transfer information. A change in the nerve terminal then triggers the release of the neurotransmitter (chemical transmission) into the synapse. Information is then received from the dendrites of connected neurons. Specifically, the depolarisation, which passes through the axon, triggers the opening of voltage dependent calcium channels in the axon terminal. This rise in calcium

concentration then triggers the movement of synaptic vesicles, which contain the neurotransmitter, to the pre-synaptic membrane where they fuse and release the transmitter into the synaptic cleft (exocytosis). Receptors on post or pre-synaptic membrane bind with the transmitter, which triggers intracellular, often second messenger mediated, processes that can be excitatory or inhibitory (the process will be explained in more detail for the neurotransmitter noradrenaline later in the chapter). The mammalian central nervous system contains several different neurotransmitters (e.g., dopamine, noradrenaline, serotonin), and co-transmitters. According to Dale's Law an individual neuron seems only to be capable of releasing one major neurotransmitter (for example, noradrenaline). However, the effect of the neurotransmitter will then depend on the nature of the receptor upon which it acts. The complexity of transmitter action is phenomenal (Leonard, 2003) also due to the fact that most neurons are interconnected and may be influenced by more than one transmitter. Similarly, in fact, most neurones release more than one neurotransmitter. For example, serotonin neurones can also release the peptide TRH.

The Neurotransmitter Noradrenaline (NA) and the Noradrenergic system

NA belongs to the chemical class of catecholamines and is synthesised from the amino acid precursors Phenylalanine and Tyrosine (See Figure 1.2).

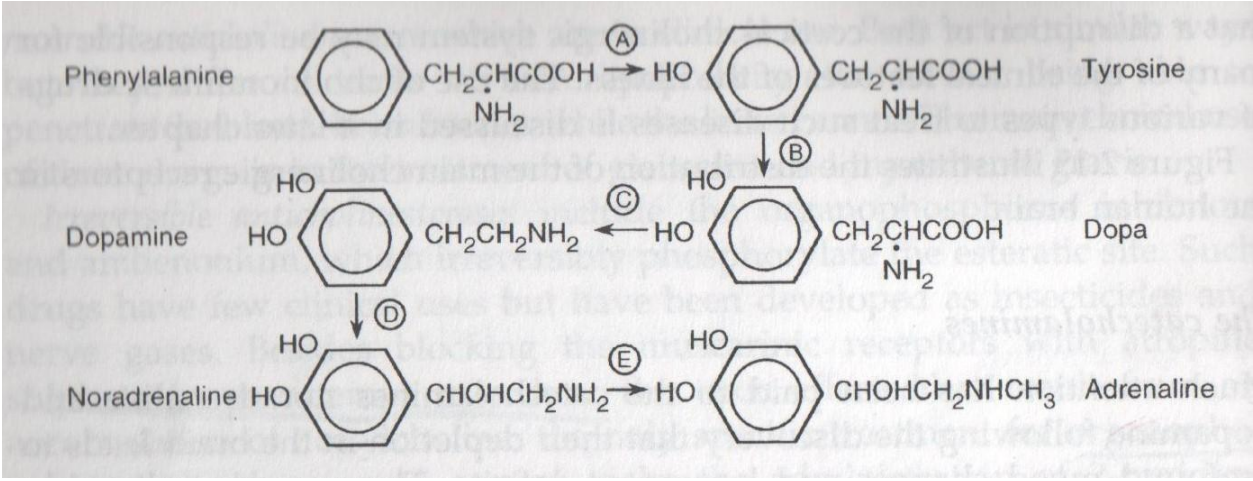


Figure 1.2 Biosynthesis of Noradrenaline. From "*Fundamentals of Psychopharmacology*" by B.E. Leonard, 2003, Wiley & Sons Ltd.: Chichester, p. 15.

In molecular biology special ligand receptor binding studies are used to determine the distribution of neurotransmitters in various brain regions (Leonard, 2003). For example, radioactive ligands (agonists or antagonists) bind with receptors, and thereby enable the researcher to determine the quantity of radioactive ligand that has been specifically bound in the brain sample tissue examined. It was determined that NA, which is released together with adrenaline from the adrenal gland, was the main catecholamine in postganglionic nerves and parts of the central nervous system. Figure 1.3 shows the central noradrenergic brain system.

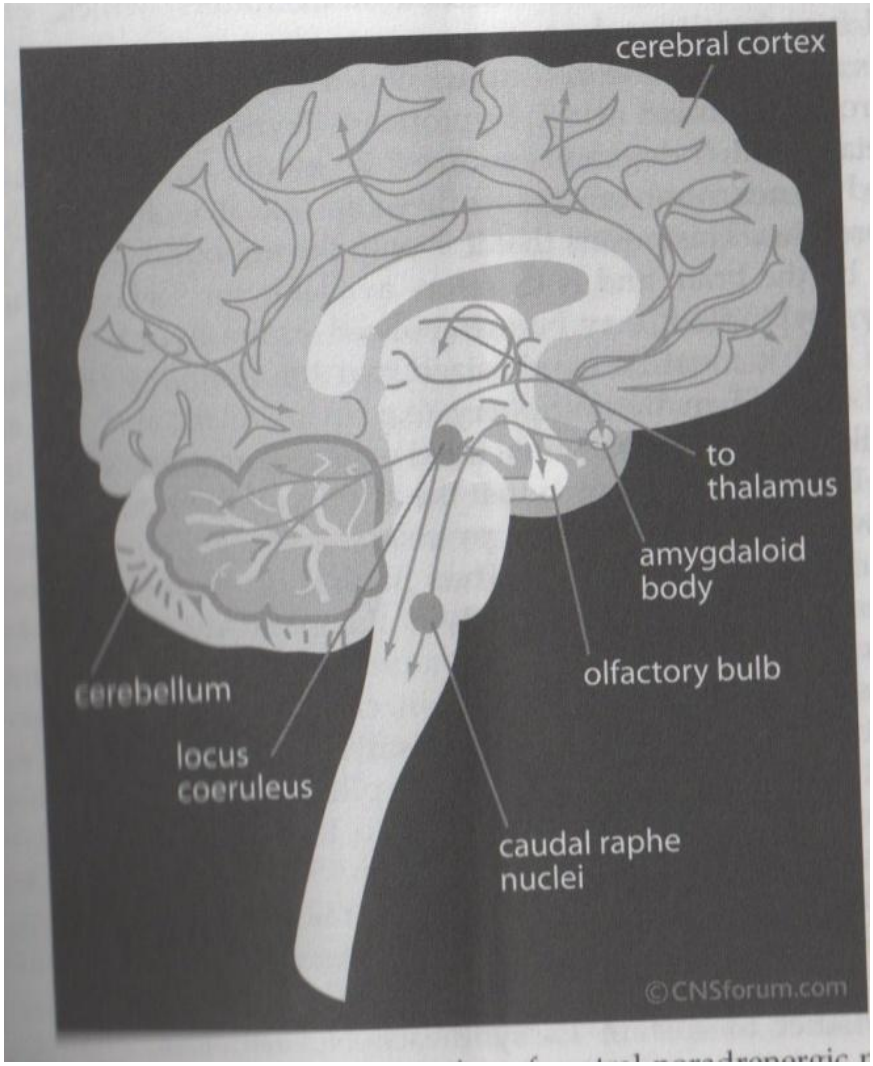


Figure 1.3 Central noradrenergic system. From "*Fundamentals of Psychopharmacology*" by B.E. Leonard, 2003, Wiley & Sons Ltd.: Chichester, p. 15.

In the brainstem NA neurons populate in the medulla oblugata and the dorsal vagal nucleus with further projections to the spinal cord, and mainly function to control blood pressure and flexor muscles (Leonard, 2003). High density of NA cells can also be found in the locus coeruleus to innervate thalamus, dorsal hypothalamus, hippocampus and cortex. The ventral NA bundle, caudally to the locus coeruleus, is connected to subcortical limbic regions.

NA plays an important role in emotional arousal and, in particular, in "fight or flight" responses to acute stressors (e.g., Fuxe, 1965). In addition, studies on experimental animals found that various stressors (e.g., extreme temperatures, foot shock) significantly and selectively reduce brain NA concentration, whilst dopamine and serotonin levels seem to be unaffected (e.g., Bliss, Ailion, & Zwanziger, 1968; Corrodi, Fuxe, & Hokfelt, 1968). For example, exposure to inescapable shock/ stress led to net deficit in brain noradrenaline levels (e.g., Weiss, 1971), suggesting increased release and utilisation of noradrenaline. Also, Galvin (1985) found that acute stressors elevated levels of the NA metabolite, MHPG in limbic regions. This net increase was correlated with plasma cortisol elevation a hormone known to be released during stressful experiences. Thus, Galvin (1985) concluded that most evidence supported the notion that noradrenaline is involved in stress responses, stress pathology, and consequences of stress exposure.

Beta receptors and Beta blocking agents

Beta adrenoceptors bind catecholamines, specifically noradrenaline and adrenaline (Opie & Poole-Wilson, 2005). Adrenoreceptors (in α- and β form) are metobotropic G-protein-coupled receptors. Within the beta receptors β1, β2, and β3 subtypes, with different pharmacological characteristics and physiological roles have been identified. Figure 1.4 shows the signal transduction for beta receptors in the example of beta receptors situated on the cardiac sarcolemma.

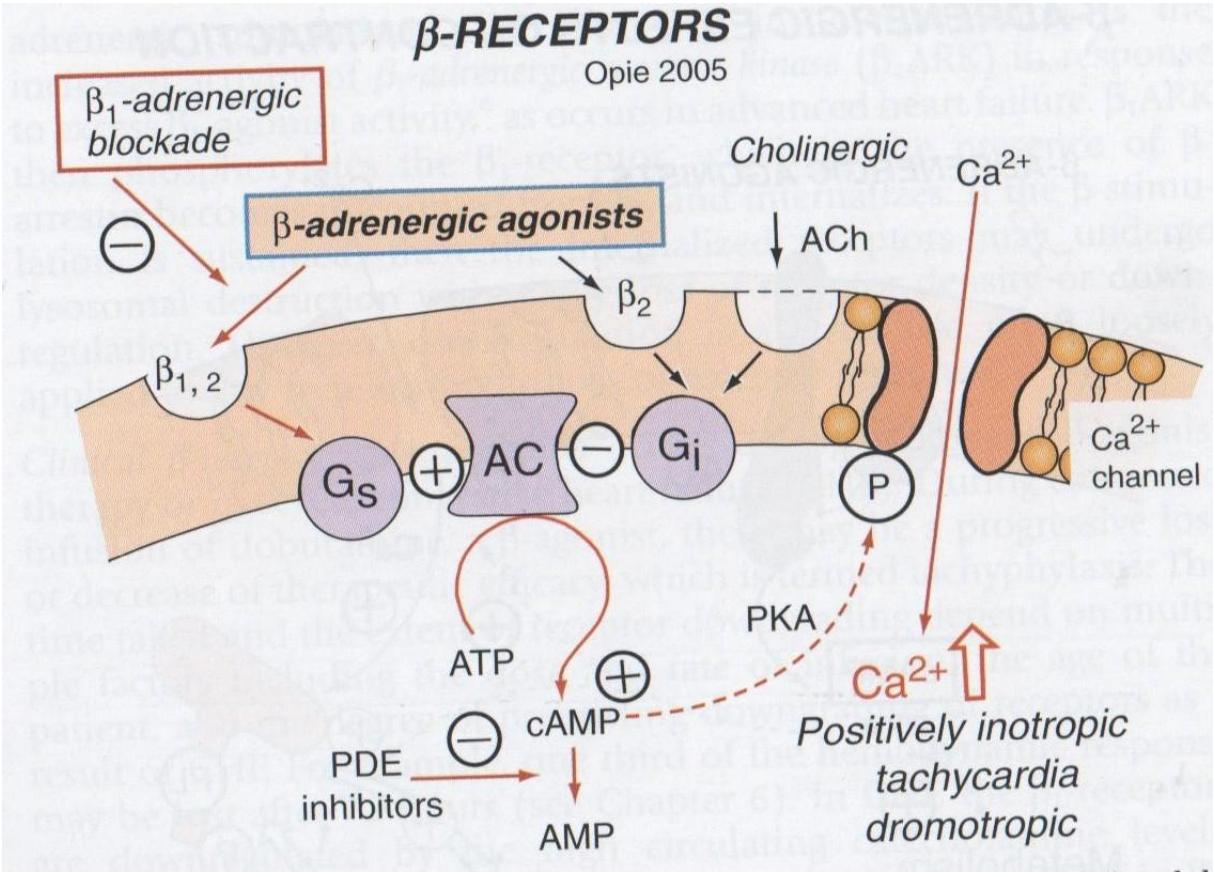


Figure 1.4 Beta receptor signal transduction on the cardiac sarcolemma. From "Beta blocking agents" by Opie, L.H. & Poole-Wilson, P.A. (2005) In: Opie L.H. & Gersh, B.J. (Eds.) *Drugs for the Heart.* 6th Edition. Elsevier: Philadelphia, p.5.

B-adrenergic agonists signal, via the stimulated G-protein that couples adenyl cyclase (AC) to the beta-adrenergic receptor, the conversion of ATP to cyclic AMP (cAMP) (the second messenger). cAMP activates protein kinase A (PKA) to phosphorylate the calcium channels to increase intracellular calcium (Ca2+) concentration. Whilst peripheral beta receptors are inhibitory and excitatory (as part of the sympathetic nervous system), brain beta receptors are suggested to mostly have excitatory effects (Leonard, 2003). For example inhibitory effects are produced on smooth muscle, whilst excitatory (positive chrono-and inotropisms) are observed in the heart. Joyce et al. (1992) examined the distribution of beta-adrenoreceptors in the rat brain and also non-diseased control human tissue. Table 1.1 gives an overview of the distribution of beta 1 and beta 2 receptors in healthy human brain tissue. The study also confirms previous findings that in the primate beta 2 receptors predominate in certain limbic structures, such as the hippocampus and amygdala (e.g., De Paermentier, Cheetham, Crompton, & Horton, 1989).

Brain region	Total	β_1	β_2	$\beta_1 + \beta_2$
Frontal cortex (Area 9)				
Layers I, II	21 ± 2	13 ± 3	9 ± 4	22 ± 2
Layers III, IV	19 ± 3	12 ± 3	8 ± 2	20 ± 2
Layers V, VI	16 ± 3	10 ± 3	7 ± 2	17 ± 3
Basal ganglia				
Caudate nucleus	22 ± 2	18 ± 2	5 ± 2	23 ± 2
Putamen	32 ± 3	26 ± 2	5 ± 2	31 ± 2
Nuc. acb. septi	28 ± 2	24 ± 2	5 ± 2	29 ± 2
Globus pall. ext.	16 ± 2	12 ± 2	5 ± 2	17 ± 2
Globus pall. int.	9 ± 2	9 ± 2	5 ± 2	14 ± 2
Amygdala				
Entire	12 ± 6	5 ± 1	8 ± 3	13 ± 3
Basal	15 ± 4	8 ± 2	8 ± 2	16 ± 2
Thalamus				
ld, medial, vl	16 ± 3	6 ± 2	10 ± 2	16 ± 2
vpl, cm, ret	17 ± 3	3 ± 1	15 ± 2	18 ± 2
Motor cortex				
Layers I, II	10 ± 2	9 ± 3	1 ± 1	10 ± 2
Layers III	8 ± 2	7 ± 3	1 ± 1	8 ± 2
Layers V, VI	9 ± 2	5 ± 2	3 ± 2	8 ± 2
Parietal cortex				
Middle				
Layers I, II	19 ± 2	15 ± 2	2 ± 1	17 ± 2
Layers III, IV	15 ± 2	12 ± 2	3 ± 1	15 ± 2
Layers V, VI	14 ± 2	8 ± 2	6 ± 2	14 ± 2
Inferior				
Layers I, II	21 ± 2	20 ± 3	2 ± 1	22 ± 2
Layers III, IV	17 ± 2	14 ± 2	4 ± 1	18 ± 2
Layers V, VI	15 ± 2	11 ± 2	6 ± 1	17 ± 2
Occipital temporal cortex				
Layers I, II	27 ± 5	22 ± 3	4 ± 1	26 ± 2
Layers III, IV	17 ± 4	13 ± 3	5 ± 1	18 ± 2
Layers V, VI	15 ± 4	9 ± 2	8 ± 2	17 ± 2
Parahippocampal gyrus				
Layers I, II	14 ± 3	8 ± 2	5 ± 1	13 ± 2
Layers III, IV	10 ± 2	3 ± 1	6 ± 1	9 ± 2
Layers V, VI	12 ± 2	2 ± 1	11 ± 2	13 ± 2
Hippocampus				
Subiculum	17 ± 6	3 ± 3	14 ± 4	17 ± 4
CA1	24 ± 9	6 ± 3	20 ± 6	26 ± 4
Dentate	27 ± 8	5 ± 3	24 ± 7	30 ± 7
Red nucleus	14 ± 4	2 ± 1	12 ± 4	14 ± 3
Substantia nigra	19 ± 3	12 ± 2	6 ± 2	18 ± 2
Cerebellum	12 ± 3	4 ± 2	9 ± 2	13 ± 2

*The values shown are the mean ± the standard deviation for all control cases (n = 12).

Table 1.1 Distribution of beta receptors in the human post-mortem brain. From "Distribution of Beta-Adrenergic Receptor Subtypes in Human Post-Mortem Brain: Alterations in Limbic Regions of Schizophrenics." by Joyce, J.N., Lexow, N., Kim, S.J., Artymyshyn, A., Senzon, D.L., Cassanove, M.F., Kleinman, J.E., Bird, E.D., Winokur, A. (1992) *Synapse*, 10, 228-246, p. 240.

Since NA is involved in peripheral and central emotional arousal and stress responses (Bliss et al., 1968; Corrodi et al., 1968; Fuxe, 1965; Galvin, 1985), and since beta receptors, situated in limbic regions, mediate noradrenergic responses, beta blocking agents should reduce emotional arousal in humans.

The beta blocker propranolol is non-selective for β1 and β2 receptors. However, compared to other beta blockers propranolol also has high lipid solubility (i.e., Octanol-water distribution coefficient; ph 7.4, 37C =>10). Therefore propranolol can cross the blood-brain barrier (a barrier of tight junctions between endothelial cells that separates cerebrospinal fluid and extracellular fluid) and have additional effects by blocking beta receptors in the CNS. Buffalari and Grace (2007) studied the effect of propranolol on the basolateral amygdala using single unit neuronal recordings in rats. They found that in vivo noradrenaline enhances tonic excitatory effects via beta receptors in the basolateral amygdala, whilst beta adrenergic blockade led to a decrease in spontaneous firing rate.

Several studies have shown that single doses of propranolol also influence emotional processing in humans (Hurlemann et al., 2010; van Stegeren et al., 2005), and that propranolol reduces physiological markers of high arousal (heart rate, potentiated startle response) following emotion-evoking stimuli (Davis Falls, Campeau, & Kim, 1993; Mills & Dimsdale, 1991;). In addition, functional neuroimaging studies have shown that propranolol leads to a reduction in amygdala responses to emotional pictures or emotional facial expressions (Hurlemann et al., 2010; van Stegeren et al., 2005). Although propranolol was originally developed for hypertension, its inhibitory effect on emotional arousal also makes it an effective and widely used treatment for stress, acute anxiety, and performance anxiety (e.g., Tyrer & Lader, 1974), though the relative contributions of central versus peripheral effects are unclear. However, recent research has suggested that, by reducing the consolidation of emotional memory, propranolol might also be an effective

treatment for post-traumatic stress disorder (PTSD), whether by being administered before exposure to a potentially traumatic situation or immediately afterwards (Mills & Dimsdale, 1991; Pitman et al., 2002; Stein, Kerridge, Dimsdale, & Hoyt, 2007).

Reboxetine and NA potentiation

Having studied propranolol, which is a means of decreasing NA transmission and emotional arousal through beta receptor blockade, the opposite pharmacological effect - which is NA potentiating - should also be researched. Ideally one would study a beta receptor agonist, which like propranolol would activate both β1 and β2receptors. Non-selective beta agonists are available; an example is the cardiac stimulant isoprenaline. However neither isoprenanline nor the more selective beta agonists which are used to treat asthma, for example salbutamol, cross the blood brain barrier. Therefore the effects of reboxetine, a selective noradrenaline re-uptake blocker which is marketed as an antidepressant were considered. Because reboxetine increases synapatic levels of NA it will indirectly activate both postsynaptic alpha and beta receptors and therefore, in terms of the receptors whose actions are influenced, it will have a broader spectrum of action than propranolol (Gilman, 1996). Single doses of reboxetine in healthy volunteers have been shown to produce a positive bias in implicit emotional processing in terms of facial expression recognition and emotional memory (Harmer, Perrett, Cowen, & Goodwin, 2001; Norbury, Mackay, Cowen, Goodwin, & Harmer, 2008). Also, in contrast to propranolol, acute reboxetine increases heart rate, presumably through stimulation of cardiac β1 receptors (Harmer et al., 2001; Norbury et al., 2008). It is therefore likely that, overall, reboxetine should increase emotional arousal.

General Hypothesis

The key question of the thesis regards the role of basic emotions in moral and social judgements. Noradrenaline is involved in basic emotional arousal and fear responses. Beta blockers such as propranolol block noradrenergic transmission both centrally and peripherally. If emotional arousal is indeed causally relevant to performance of moral and social judgments then manipulating noradrenergic transmission should affect racial bias evaluations and moral decisions. As noted above, emotions are thought to be relatively more involved in rapid, implicit phases of decision making. Therefore, specifically implicit and not explicit attitudes are expected to be affected by noradrenergic manipulation, as are personal but not impersonal moral decisions.

In the following four chapters, four psychopharmacological experiments and a pharmacological fMRI study will be presented that manipulate noradrenaline function in order to explore the causal role of basic emotional arousal in attitudes and moral judgments.

CHAPTER 2: BETA ADRENERGIC BLOCKADE REDUCES UTILITARIAN JUDGMENT

Introduction

The present study investigated the relation between propranolol and moral decision-making. This relation is of considerable practical interest, but it might also shed new light on the important theoretical debate about the role of emotion in moral decision-making (Huebner et al., 2008). It has been argued that deontological moral judgments are based on a pre-potent emotional aversion to harming others, but that this emotional response can sometimes be overcome with effort, leading to a more reason-based utilitarian response (Greene et al., 2004; Greene, 2008). In line with this hypothesis, patients with damage to the VMPC exhibit increased utilitarian judgment in response to high conflict personal dilemmas compared to healthy individuals, a finding which has been attributed to a deficit in social emotion (Ciaramelli, Mucciolo, Ladavas, di Pellegrino, 2007; Koenigs et al., 2007). In addition, Moretto, Ladavas, Mattioli, and di Pellegrino, (2009) report that healthy individuals, but not patients with VMPC damage, showed a skin conductance response (SCR), a somatic marker of affective arousal, before making utilitarian judgments in personal dilemmas. Moreover, this anticipatory SCR was negatively correlated with the frequency of such utilitarian judgments in healthy individuals.

This research suggests that aversion to harm in personal moral dilemmas is at least partly mediated by emotional arousal. Since propranolol has been consistently shown to reduce noradrenergic mediated physiological arousal (e.g., Hurlemann et al., 2010), it offers a means to investigate the role of such arousal in moral judgment. I hypothesized that if deontological judgments against personal harm are based in an immediate negative

affective response then propranolol should lead to an increase in utilitarian judgment compared to placebo (Levy, 2007). The present study was designed to assess this hypothesis by investigating the effect of a single dose of propranolol on moral decision-making in healthy volunteers.

Method

Subjects

Forty subjects (M_{age} = 24.30; 20 male and 20 female students) were recruited via poster and newspaper advertisement. Subjects were instructed to refrain from alcohol or coffee 24 hours before the study. Full written consent was obtained from all subjects and the study was approved by the Oxford NHS ethics committee.

Procedure

Individuals were first screened to exclude those with any medical contraindication for propranolol (e.g., asthma, low blood pressure). Subjects with any past or present axis 1 psychiatric disorder, as measured using the Structured Clinical Interview for DSM-IV (SCID-IV) (Frances, First, & Pincus, 1995) were also excluded (See Appendix 2.1 for the case record form for more details about the screening). Propranolol (40 mg) or placebo was administrated in identical capsules in a parallel group design in which each subject was randomised to receive either propranolol or placebo in a double blind manner. Subjects' pulse rate was recorded using a pulse oximeter. Measures were obtained immediately prior to tablet administration, and at 30 min intervals following that. Additionally, subjects' mood was assessed using visual analogue scales (0-10 anchors; 0 = *not at all* and 10 = *extremely*) at three time points (before, 60 min after, and 150 min after propranolol/placebo

administration) in which subjects rated how sad, happy, alert, tired, angry, or anxious they felt (See Appendix 2.2).

The moral decision task was presented on the computer using E-prime software (Version 2.0) 90 min after propranolol/placebo administration. The task included 20 hypothetical moral dilemmas, drawn from Koenigs et al. (2007) (see Appendix 2.3 materials for a full list of moral dilemmas). Of these, 15 were 'personal' (i.e., involving 'up-close-and-personal' harm) and 5 were 'impersonal' (based on Greene et al., 2001). Personal dilemmas were mostly 'high conflict' dilemmas (N = 13), on which there is no general consensus about the answer (as classified by Koenigs et al., 2007; see also Kahane & Shackel, 2010). Of the 15 personal dilemmas, 7 described scenarios where the victim of the proposed harmful act would inevitably die even if this act was not chosen (Huebner, Hauser, & Pettit, 2011). All dilemmas were presented in random order.

Subjects read the dilemmas on screen in their own time, and responded using the keypad. Subjects were asked to rate how morally acceptable the action was on a 6-point scale (0 = *completely morally unacceptable* and 5 = *completely morally acceptable*), and whether they would themselves perform this action (0 = *absolutely not* and 5 = *absolutely yes*). Subjects' responses and their response times were recorded. Response times were recorded from the onset of the question to the key press/reply.

Results

Demographic data, heart rate

Independent sample *t*-tests revealed that the propranolol and placebo group did not differ in age, or body mass index (both *ps* > .05). Repeated measures analyses of variance (ANOVAs) for the six mood ratings from the visual analogue scales showed that there

were no differences in reported mood between the propranolol and placebo group at any time (all $p > .05$).

A 2 Treatment (propranolol versus placebo) x 5 Times repeated measure ANOVA was conducted to assess heart rate change (difference in heart rate from the baseline recording). A significant interaction of Time and Treatment was found ($F(4,35) = 9.27$, $p = .00$). Post hoc *t*-tests showed that the decrease in heart rate was significantly greater in the propranolol as compared to the placebo group at 90 min ($t(38) = -2.54$, $p = .02$) and 120 min ($t(38) = -2.50$, $p = .02$) after treatment (see Figure 2.1).

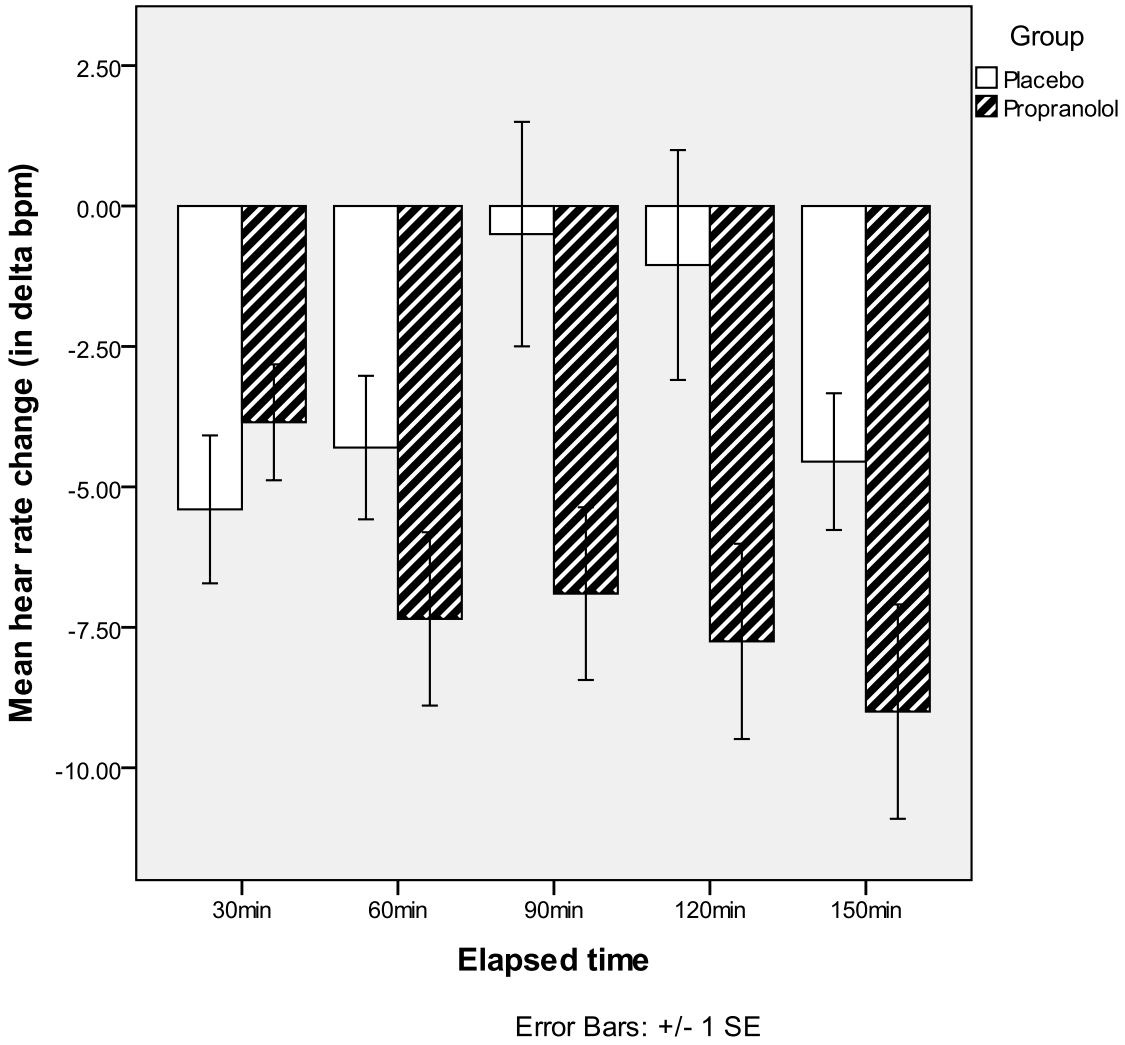


Figure 2.1 Heart rate change in propranolol and placebo group.

Moral judgments

For moral judgment responses two different averages (one for the 15 personal dilemmas and one for the 5 impersonal dilemmas) were calculated. The Kolmogorov-Smirnov test showed that the sample was not normally distributed ($p < .05$). Therefore data were log transformed, and three sub-scores from the placebo group, which were detected as outliers, were excluded. This led to optimal Kolmogorov-Smirnov tests for personal and impersonal dilemmas in placebo and propranolol group (all $p > .20$).

I conducted separate ANOVAs for the moral acceptability question (Is the action morally acceptable?) and for the performance question (Would you perform the action?).

Moral acceptability question First, a 2 Treatment (propranolol versus placebo) x 2 Dilemma type (personal vs. impersonal) mixed ANOVA was conducted on the moral acceptability question. I found a main effect of dilemma type ($F(1,35) = 123.39$, $p < .00$). I also found a significant Dilemma type X Treatment interaction ($F(1,35) = 5.20$, $p = .03$). Individuals generally rated the proposed action in personal dilemmas as less morally acceptable than in impersonal dilemmas ($t(36) = -7.83$, $p < .00$; $t(39) = 12.00$, $p < .00$). Importantly, subjects in the propranolol group rated actions as less morally acceptable ($M = .27$, $SD = .28$) than did subjects in the placebo group ($M = .43$, $SD = .11$) in personal ($t(37) = 2.18$, $p = .04$; $d = .72$) but not in impersonal ($t(37) = 1.07$, $p = .29$) moral dilemmas (see Figure 2.2).

Moral performance question A 2 Treatment (propranolol vs. placebo) x 2 Dilemma type (personal vs. impersonal) mixed ANOVA was also performed on the performance question. This revealed a main effect of Dilemma type ($F(38,1) = 147.20$, $p < .00$), but no interaction of main effect with Treatment (all $p > .20$). Overall individuals were more

likely to rate that they would perform the action in impersonal (M = .56, SD = .07) as compared to personal moral dilemmas (M = .25, SD = .20), ($t(39) = 12.00$, $p < .00$).

There was a significant correlation between the answers to the moral acceptability question and the performance question ($r(40) = .53$, $p = .00$). However, individuals generally rated the moral acceptability of the proposed act as higher than they rated their willingness to actually perform this act. This was the case both for personal ($t(39) = 2.95$, $p = 0.01$) and for impersonal moral dilemmas ($t(38) = 3.12$, $p = 0.00$).

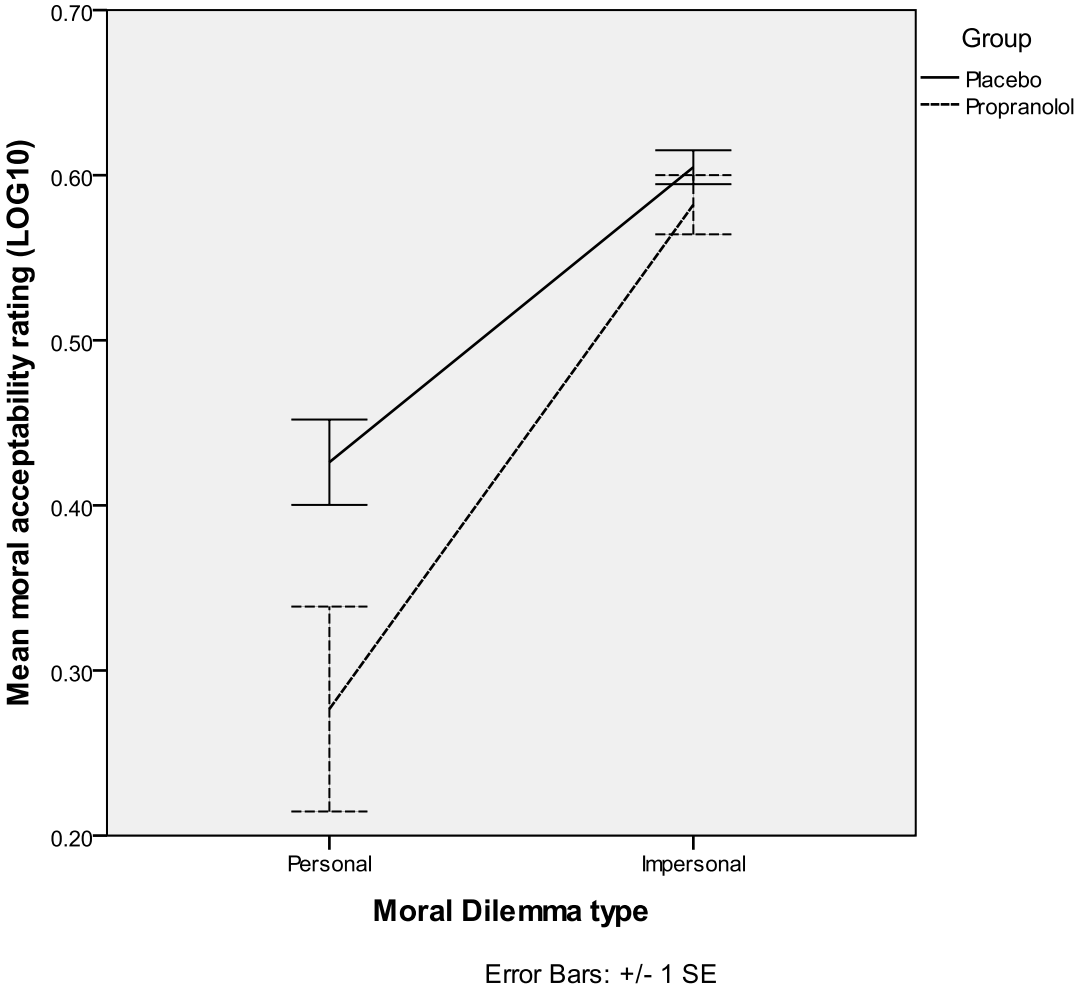


Figure 2.2 Mean moral acceptability ratings for personal and impersonal moral dilemmas in propranolol and placebo group.

Response Times A 2 Treatment (propranolol versus placebo) x 2 Dilemma type (personal versus impersonal) mixed ANOVA was also computed for response times first for the acceptability question. I found a significant main effect of Dilemma type ($F(1,38) = 4.65$, $p = .04$). The Dilemma type and Treatment interaction was found to be significant ($F(1,38) = 5.94$, $p = .02$). Individuals in the placebo group took significantly longer to rate the moral acceptability of acts in personal ($M = 7517.21$, $SD = 2596.02$) as compared to impersonal ($M = 6374.09$, $SD = 2139.90$) dilemmas ($t(19) = -2.58$, $p = .02$). For the propranolol group the difference in response time for personal ($M = 6519.6533$, $SD = 2041.58$) and impersonal ($M = 6424.61$, $SD = 2011.10$) dilemmas was not significant ($p > .05$) (see Figure 2.3). In addition, there were no response time differences for the performance question.

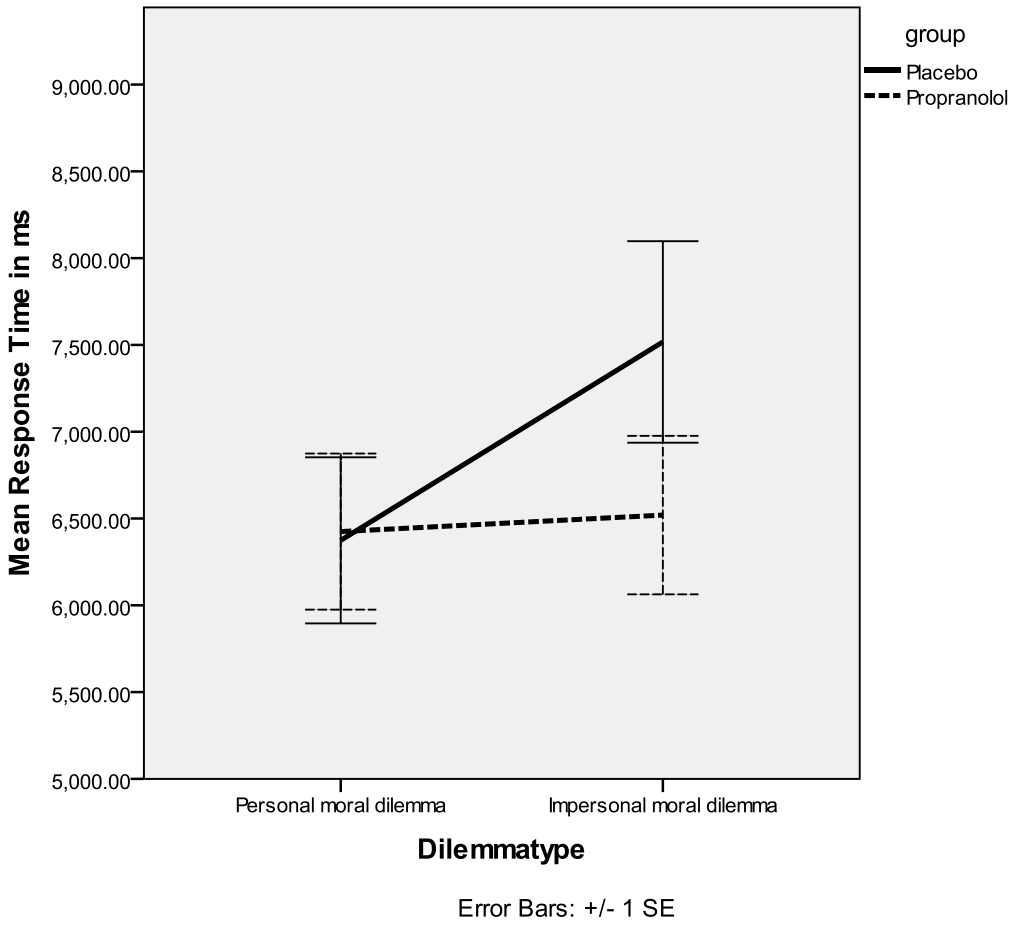


Figure 2.3 Response times for personal and impersonal moral dilemmas in both groups.

Working memory capacity, gender effects A previous study has reported a positive correlation between working memory capacity and utilitarian judgment in personal dilemmas (Moore et al., 2008), but only in dilemmas where the act endorsed (e.g., killing one person to save five others) would not make the person harmed worse off, because they would inevitably suffer this harm (because, for example, everyone would die if one doesn't act; Huebner et al., 2011). Since some studies have suggested that propranolol can reduce working memory capacity (Chamberlain, Mueller, Blackwell, Robbins, Sahakian, 2006), I controlled for this possible influence by performing a 2 Treatment (propranolol versus placebo) x 2 Dilemma type (inevitable versus non-inevitable harm) mixed ANOVA. This could then account for the effect, since the effect of working memory was only found on moral dilemmas of the inevitable type. Therefore if the propranolol effect was caused by changes in working memory, it would also be likely that the effect would only be observed on the moral dilemmas that were of the inevitable type. However, there was no main effect or interaction for Dilemma type (all $p > .20$). In addition, I found no effect or co-variance of gender with any of the observed effects (all ps > .20).

Moral decisiveness Finally, I investigated whether individuals in the propranolol group were more decisive in their judgments. Scores of 2 or 3 on moral judgments were categorised as indecisive (i.e., neither clearly deontological nor utilitarian), and scores of 0 or 1 and 4 or 5 as decisive (i.e., clearly deontological or utilitarian). On average, subjects in the propranolol group made 29.3% indecisive judgments, compared to 40.7% in the placebo group. A Mann Whitney U-test confirmed that individuals in the propranolol group made more decisive judgments ($U = 123.00$; $z = -2.10$, $p = .04$) in personal moral dilemmas.

Discussion

Suppression of noradrenergic-mediated arousal by propranolol was associated with a significant difference in moral judgment compared to placebo. However, contrary to the hypothesis, propranolol led to an increase in deontological, not utilitarian, judgment.

Propranolol in single doses is a well-established technique to assess the role of noradrenaline pathways in emotional responses (Harmer et al., 2001; Hurlemann et al., 2010). Although I found no significant difference in self-reported mood between the propranolol and placebo groups, heart rates in the propranolol group were significantly lower, suggesting a reduction in physiological arousal, in line with numerous previous studies (Hurlemann et al., 2010; van Stegeren et al., 2005). My results thus suggest that general physiological arousal is not likely to play an essential role in generating deontological judgments, though these results cannot rule out that deontological judgments involve secondary emotions such as guilt, which may be based more in cognitive appraisal than in physiological arousal (Johnson-Laird & Oatley, 1992). Moreover, further research using a peripherally acting beta-adrenoceptor antagonist is needed to determine whether the observed effect of propranolol on moral decision making is due to central beta-adrenoceptor blockade or to antagonist effects in the peripheral sympathetic nervous system. In addition, more sensitive measures of heart rate and other markers of physiological arousal are needed to investigate the temporal course of emotional arousal when individuals under propranolol are engaged with moral dilemmas.

Further research is also needed to clarify why a reduction in noradrenergic-mediated arousal leads to an increase in deontological judgment. At present I can only speculate about several possible explanations.

Previous studies have shown that propranolol reduces the discrimination between large and small possible losses in a gambling task when the probability of winning was relatively low and the probability of losing was high (Rogers, Lancaster, Wakeley, & Bhagwagar, 2004). Since personal moral dilemmas can be understood as involving a choice between two options that involve highly probable (or even certain) loss of life, it might be suggested that subjects under propranolol were exhibiting a similar lack of discrimination between differences in magnitude of overall loss. However if propranolol generally reduced concern for consequences, it should affect responses to both personal and impersonal dilemmas, whereas I observed an increase in deontological judgment only in personal dilemmas.

A second possibility is that propranolol led to an increase in aversion to harming others. This is in line with extensive evidence that propranolol reduces aggression (Greendyke, Kanter, Schuster, Verstreate, & Wootton, 1986; Silver et al., 1999). This would explain why propranolol only affected responses to personal dilemmas. Interestingly, a decrease in aggression has also been associated with selective serotonin reuptake inhibitors such as citalopram (Armenteros & Lewis, 2002; Vartiainen et al., 1995), which have recently also been shown to increase deontological judgment (Crockett et al., 2011). It is of interest that Crockett et al. (2011) report that a single dose of the noradrenaline re-uptake inhibitor, atomoxetine, failed to influence moral judgement, whereas from my findings a decrease in deontological judgements might be expected. However, atomoxetine would be expected to facilitate neurotransmission at both alpha and beta adrenoceptors; hence its effect on moral decision-making might not be simply contrary to that of propranolol. It should also be noted that the Crockett et al. study employed a cross-over design while I used a parallel group method. While my design avoids the issue of learning effects, it is open to the objection that the findings may be

confounded by baseline differences between the two groups. I tried to minimise this possibility by careful demographic matching of the treatment groups but it would be of interest to see if my findings can be replicated in a cross-over design.

It is also intriguing that although propranolol increased rates of deontological judgment in personal dilemmas, it did not have a parallel effect on subjects' willingness to perform the proposed act. This difference may, however, reflect a floor effect, given that most subjects were already generally averse to actually performing harmful acts even when they rated them morally acceptable.

Another result that needs to be explained is the increase in decisiveness in moral judgment, coupled with a decrease in response time in personal dilemmas, compared to the placebo group. These findings are in line with previous research suggesting that deontological judgments in such dilemmas are based on an intuitive response (Cushman, Young, & Hauser, 2006; Kahane, Wiech, Shackel, Farias, Savalescu, & Tracey, *in press*). It can be suggested that subjects under propranolol engaged in less deliberation, and were more confident of their immediate responses than subjects who took placebo. Although propranolol can impair working memory (Chamberlain et al., 2006), this is unlikely to explain this effect, since the only study so far to establish a direct relation between working memory capacity and utilitarian judgment found such a relation only in dilemmas where the personal harm was inevitable (Moore et al., 2008) and such a selective effect was not observed in the present study. In addition, a reduction in working memory would also be expected to affect responses to impersonal dilemmas. Another possibility is that in the absence of affective cues, the responses of individuals were guided instead by explicit rules such as 'do not directly harm others', which might be especially salient in personal dilemmas. However this suggestion is incompatible with the finding that damage to the VMPC, which is associated with emotional blunting, leads rather to an increase in

utilitarian judgment in high conflict personal dilemmas (Koenigs et al., 2007). It is thus more likely that an increase in aversion to harming caused the deontological response to strongly dominate decision-making, leading both to an increase in deontological judgment and to faster and more decisive responses. In addition, it is possible that the reduction in anxiety that is associated with propranolol (Tyrer & Lader, 1974) also played a role in increasing judgment confidence.

Although further research is needed to clarify the exact role of noradrenergic arousal in moral judgment, this study provides some evidence that propranolol, a widely used drug, can influence moral decision-making. This finding is especially important in the context of the ongoing debate about the potential use of propranolol in the prevention or treatment of post-traumatic stress disorder in military or rescue service personnel (Henry, Fishman, Younger, 2007), given that the hypothetical dilemmas used in the present study involve difficult decisions in extreme emergency situations.

CHAPTER 3: PROPRANOLOL REDUCES IMPLICIT RACIAL BIAS

Introduction

This study employed propranolol to test the hypothesis that emotional responses influenced by noradrenergic transmission play a mediating role in implicit but not in explicit forms of racial bias. It was previously suggested that implicit prejudice might have a stronger emotional component. For example fMRI research demonstrated that the amygdala activity to unfamiliar black faces was correlated with the implicit – but not the explicit – racial bias (e.g., Phelps et al., 2000; see also Chapter 1 for a detailed discussion). Propranolol intervention was employed as a means to reduce noradrenergic mediated emotional arousal, to determine the causal role of such arousal in intergroup attitudes. Besides its well-established effect on emotional memory via reduction in emotional conditioning (Chamberlaine et al., 2006), functional neuroimaging studies have also shown that propranolol leads to a reduction in amygdala responses to both facial expressions and visual emotional stimuli (Hurlemann et al., 2010; van Stegeren et al., 2005). If noradrenergic medicated emotional arousal is causally relevant for the implicit racial bias β-adrenoceptor blockade should lead to a reduction in implicit racial attitudes, as measured by the IAT, without a corresponding reduction in measures of explicit prejudice.

Method

Subjects [3]

Subjects were 36 healthy volunteers who gave full informed, written consent to the study. Subjects were all of white ethnic origin, mostly from a British student population. They were screened using the same procedure as described in chapter 2.

[3] Subjects in this study were the same as those used in Study 1 (Chapter 2). Four subjects of Asian ethnicity were excluded.

Procedure

The measure of explicit prejudice measure was administered 70 min. and the IAT at 120 min, post drug treatment; this timing was based on the pharmacokinetics of propranolol with peak plasma concentrations being reached between one and two hours (Gilman, 1996) (See Chapter 2 for more details).

Tasks

Explicit prejudice measure A feeling thermometer, an established tool for measuring explicit prejudice (Converse & Presser, 1986), was used; on a 10-item scale, ranging from 10 to 100 degrees – analogous to a thermometer – subjects rated how "warm" or "cold" they felt towards various groups (10 = *cold* and 100 = *warm*). Besides white and black people, subjects also indicated their attitude towards homosexuals, Muslims, Christians, and drug addicts. Differences between the scales for in- versus outgroup ratings indicate the level of explicit prejudice (See Appendix 3.1 for the questionnaire).

Implicit association test A computerised racial picture version of the IAT was used, administrated using E-prime software (Version 2.0). The design of the task followed that of the original version used by Greenwald et al. (1998). The tasks consisted of 7 blocks, each with 20 trials. Subjects were asked to respond as quickly and accurately as possible. Subjects were asked to perform a categorisation task by sorting positive/negative words and pictures of faces from black/white individuals. Target words appeared in the centre of the screen, categories on the left/right corner. To assign items to the left category subjects pressed the "e" key, for the right category they pressed the "i" key. Blocks 1 and 5 contained positive/negative words. Block 2 black/white faces, and Blocks 3, 4, 6, and 7 combinations in randomised order (See also Appendix 3.2 for more details on the IAT). The IAT effect was determined by latency differences in the time to respond in the main

trials, Blocks 7 and 4 (e.g., prejudice congruent versus prejudice incongruent blocks), as well as in the practice trials (Blocks 3 and 6). The pictures of black and white faces, as well as positive and negative words were taken from the original test.

Results

The groups were well matched in terms of demographic measures as well as measures of mood (see Table 3.1).

Table 3.1 Demographic data for propranolol and placebo groups.

Group	**Propranolol**	**Placebo**	
Age	*M* = 22.33 *SD* = 3.94	*M* = 22.72 *SD* = 3.08	n.s.
Gender	Male *N* = 9 Female *N* = 9	Male *N* = 10 Female *N* = 8	n.s.
Ethnic Origin	White British *N* = 8 Other white European *N* = 6 White American: *N* = 3	White British *N* = 10 Other white European *N* = 5 White American *N* = 3	n.s.
Depressed mood (BDI)	*M* = 2.06 *SD* = 1.78	*M* = 2.82 *SD* = 2.43	n.s.
Neuroticism	*M* = 4.88 *SD* = 3.64	*M* = 5.18 *SD* = 2.98	n.s.

Note. Non-significant differences: all *p*s > .20

Relative to placebo, propranolol did not alter VAS ratings of any of the six emotions (no main or interactive effects on ANOVA, all *p*s > .20).

Propranolol significantly lowered heart rate (calculated as change from baseline) as shown by a significant main effect of treatment on the ANOVA ($F(4, 30) = 6.56$, $p = .02$), as well as a Time x Treatment interaction ($F(4, 30) = 4.62$, $p = .00$). Post hoc *t*-tests revealed that the heart rate change (e.g., the drop of the pulse from baseline) was significantly greater in the propranolol group (at 60 min: $M = -8.17$, $SD = 6.76$; at 90 min: $M = -7.27$, $SD = 7.16$; at 120 min: $M = -8.55$, $SD = 7.77$) as compared to the placebo group (at 60 min: $M = -3.18$, $SD = 4.74$; at 90 min: $M = -.722$, $SD = 7.16$; at 120 min: $M = -1.67$, $SD = 9.19$) (at 60 min: $t(33) = 2.51$, $p = .02$; d = -.87; at 90 min: $t(34) = 2.4$, $p = .02$; d = .78; at 120 min: $t(34) = 2.40$, $p = .02$; $d = .8$).

Since the data for explicit prejudice was not normally distributed, group differences were assessed with the Mann-Whitney U-test for independent, non-parametric data. I found no effect of propranolol on the measure of explicit racial prejudice. Additionally, no significant difference between the propranolol and placebo groups was found for religious prejudice, sexual prejudice, or prejudice against drug addicted individuals (all *p* values > .20) (See Table 3.2).

Group	**Propranolol**	**Placebo**	
Racial prejudice score	*Mean Rank* = 18.22	*Mean Rank* = 18.78	*Z* = -.20 *n.s.*
Religious prejudice score	*Mean Rank* = 19.17	*Mean Rank* = 17.83	*Z* = -.39 *n.s.*
Sexual prejudice score	*Mean Rank* = 18.81	*Mean Rank* = 18.19	*Z* = -.20 *n.s.*
Prejudice score: Drug addicted individuals	*Mean Rank* = 16.58	*Mean Rank* = 20.42	*Z* = -.12 *n.s*

Table 3.2 Explicit prejudice ratings for both groups: a Mann-Whitney U-test revealed no significant differences in explicit prejudice.Note. Non-significant results: $p > .20$

The IAT was analysed according to the improved algorithm as provided by Greenwald, Nosek, & Banaji, (2003). In this method, the main trials (Blocks 4 and 7) as well as the practice trials (Blocks 3 and 6) are analysed. First, error latencies were replaced by the mean response time for correct trials + 600 ms. Only data from blocks with less than 15% errors were analysed (1 subject was excluded due to more than 20% errors on practice and main trials, for 3 other subjects only the main trials were analysed due to too many errors in the practice trials).

The two differences between Blocks 4 and 7, and 3 and 6 were divided by the pooled standard deviation for correct trials. The average of the corrected differences revealed the IAT effect. The IAT was analysed using a mixed design analysis of variance (ANOVA). The main between- subjects factor was Treatment while the within-subject factor was Congruency (congruent versus incongruent trials). The measure of the IAT reaction times showed a main effect of Congruency ($F(1,33) = 13.60$, $p = .00$) (i.e., the IAT effect), as well as a significant Congruency x Treatment interaction ($F(1,33) = 6.20$, $p =$

.02). There was no main effect of Treatment ($F(1,33) = .26$, $p = .61$). Post hoc *t*-tests revealed no significant difference between groups in mean response times (in ms) on congruent (placebo: $M = 702.98$, $SD = 86.67$; propranolol: $M = 788.72$, $SD = 175.07$) or incongruent (placebo: $M = 866.23$, $SD = 168.98$; propranolol: $M = 820.50$, $SD = 106.68$) trials ($t(33) = -1.85$, $p > .05$; $t(33) = .95$, $p > .05$). However, an unpaired *t*-test showed the difference between congruent and incongruent trials (the IAT effect) was significantly smaller in the propranolol ($M = .26$, $SD = 1.09$) as compared to the placebo group ($M = 1.02$, $SD = .84$) ($t(33) = 2.30$, $p = .03$; $d = .78$) (see Figure 3.1).

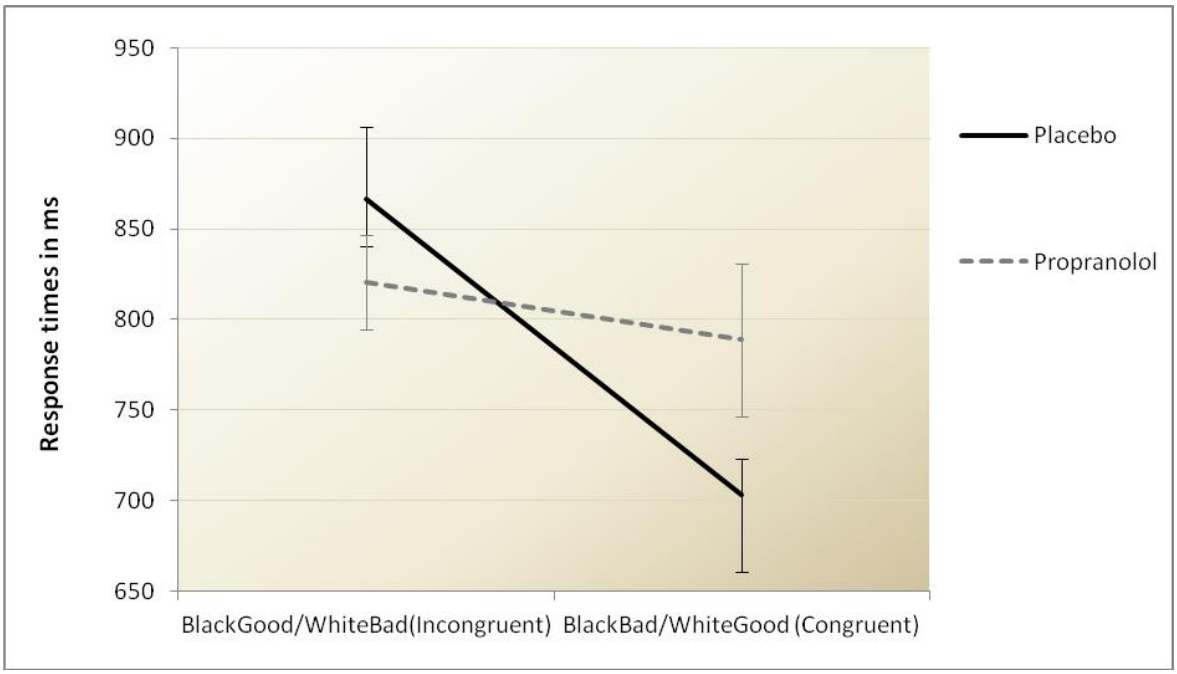


Figure 3.1 Mean response times for the IAT in congruent and incongruent blocks for placebo and propranolol group.

Paired *t*-tests also revealed that an IAT effect could be determined for both practice (M = 112.13, SD = 111.06) and main (M = 161.05, SD = 244.53) trials in the placebo group (t(17) = 4.30, p = .00; t(17) = 2.80, p = .01), but not in the propranolol group (M = -26.30, SD = 198.08; M = 65.55, SD = 153.10; t(18) = -.53, p > .05; t(18) = 1.82, p > .05). Additionally, in the propranolol group 34% of the subjects had a 'negative' IAT score (they were faster in the bias incongruent as compared to the congruent condition). In the placebo group no subject had such a score. This difference was significant ($\chi 2$(1, N = 37) = 7.20, p = .01) (See Figure 3.2).

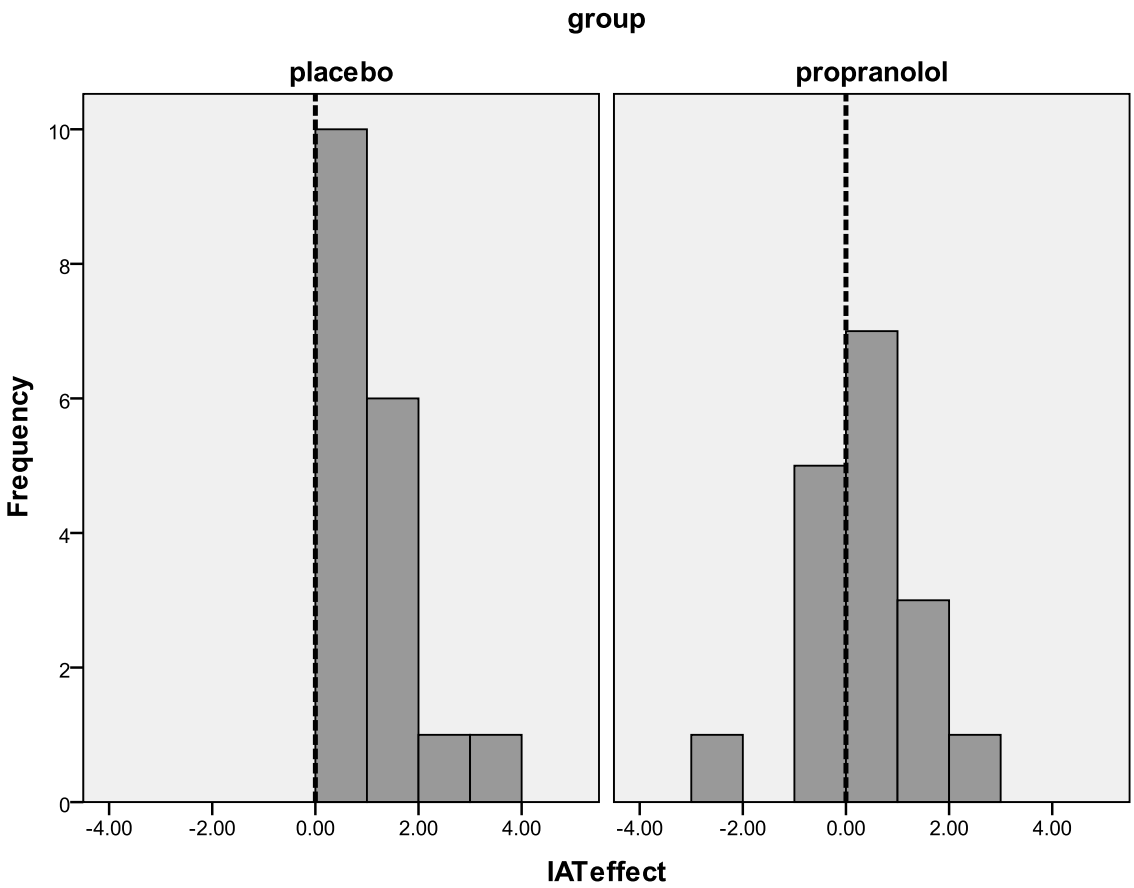


Figure 3.2 Distribution of the IAT effect for both groups.

Discussion

The main finding of this study was that propranolol significantly reduced implicit but not explicit racial bias. This supports the hypothesis that noradrenaline mediated emotional responses play a role in the generation of implicit negative racial attitudes, and confirms prior theorising suggesting a greater affective component in implicit compared to explicit attitudes (Stanley et al., 2008). Propranolol in single doses is a well-established means of assessing the role of noradrenaline pathways in emotional learning and perception (Harmer et al., 2001; Hurlemann et al., 2010). However, β-adrenoceptor antagonists have other neuropsychological effects which need to be considered in my findings. The subjective VAS ratings of subjects' mood and alertness do not suggest that propranolol caused sedation relative to placebo. In addition, it seems unlikely that the observed effect on IAT was due to a general impairing effect of propranolol on cognitive performance, given that previous research has demonstrated that propranolol and other beta blockers do not impair performance on purely cognitive conflict tasks, such as the standard Stroop test (Harvey, Clayton, & Betts, 1977; Lasser, Nash, Lasser, Hamill, & Batey, 1989). In addition, propranolol did not cause an overall slowing of reaction time in the IAT task.

Further research is needed to clarify the causal mechanisms through which noradrenergic pathways may influence implicit bias. Although this study used only behavioural measures, prior studies have shown that propranolol can reduce amygdala response to visual stimuli associated with negative emotions such as fear and anger (Van Stegeren et al., 2005) and the role of noradrenergic transmission in the basolateral amygdala in emotional processing has also been demonstrated in animal studies (McGaugh, 2000). The amygdala plays a key role in the early non-conscious appraisal of threat, and may therefore also be involved in the mediation of implicit racial prejudice. In line with this proposal, previous neuroimaging studies found that increased amygdala

activation was associated with implicit prejudice but not with explicit racial attitudes (Phelps et al., 2000). However, Phelps et al. (2003) found that a single patient with bilateral amygdala damage exhibited an intact IAT effect, leading the authors to suggest that the amygdala may not be a critical structure for the manifestation of implicit bias. Phelps et al. (2003) proposed instead that the amygdala may be involved in the acquisition of emotional bias, or that common neural pathways influence both behaviour on the IAT and responses in the amygdala to the task. It is also possible that in the presence of amygdala damage, other compensatory mechanisms may be recruited in the IAT task. It thus remains possible that automatic fear or threat responses related to amygdala activation and normally elicited by viewing of out-group faces might be the central emotional component mediating implicit attitudes. Propranolol might act at this level to produce its effect on the IAT, although further neuroimaging studies are needed to confirm reduction in limbic activation in response to such social cues following propranolol (see Chapter 5 this thesis, for such a study).

Another possibility is that the observed effect of propranolol on implicit attitudes is due to a decrease in peripheral sympathetic responses. It could be, for example, that negative implicit attitudes are triggered by somatic experiences dependent on increased sympathetic activation independent of amygdala activation. Propranolol may lead to a significant reduction in such responses, and thereby reduce the "embodied" experience of emotional responses to a racial out-group. Further studies with a peripherally acting β-adrenoceptor antagonist, such as nadolol, are needed to determine whether the action of propranolol observed here is mediated by peripheral or central mechanisms. For example, Van Stegeren, Everaerd, & Gooren, (2003) found that memory for emotional stimuli were impaired by propranolol but not nadolol, suggesting a central location for the relevant β-adrenoceptors.

The influence of propranolol on implicit attitudes observed in the present study may shed new light on the neurobiological mechanisms underlying implicit racial associations. Given the important role that implicit attitudes appear to play in overt forms of discrimination against outgroup members, and the widespread use of propranolol for medical purposes, these findings might also be of practical interest, and require careful ethical consideration (see Chapters 6 and 7, this thesis). Further research, however, is needed to clarify whether the observed effect would persist with sustained propranolol treatment, and whether propranolol can modulate implicit bias outside the laboratory.

CHAPTER 4: REBOXETINE EFFECT OF MORAL JUDGMENTS AND RACIAL ASSOCIATIONS

Study 3 Reboxetine effect on moral judgments

Introduction

The research reported earlier in this thesis proposed that noradrenaline might play a causal role in higher order psychological processes, such as moral judgments (see Chapters 2 and 3). Specifically, I found that propranolol led to an increase in deontological moral judgments (i.e., subjects rated harmful actions that have a greater future benefit (for example killing one to save five) as significantly less morally acceptable). In addition, judgments were formed faster and were also more decisive. This effect was only observed for personal moral dilemmas, which were previously suggested to be more emotionally arousing (Greene et al., 2001). This finding was in contrast to previous theorising, suggesting that deontological, compared to utilitarian, judgments have a stronger affective component. I argued that one explanation might be that primary emotional arousal might be involved in increasing harm aversion and that individuals might adhere to their basic moral principles if arousal is reduced. If noradrenergic mediated emotional arousal indeed plays a role in moral decision making then enhancement of noradrenergic transmission – compared to reduction via propranolol– might lead to opposite patterns of moral judgments. This could then deliver further evidence for the role of primary emotional arousal in higher order psychological processes.

Reboxetine was found to be the most selective noradrenergic-reuptake inhibitor (Kent, 2000). Some studies have suggested that a single dose of reboxetine might have the opposite behavioural effect to propranolol. For example De Marttino, Strange, & Dolan,

(2008) found that propranolol reduced ability to detect emotional stimuli of any valence whilst reboxetine increased it. However Onur, Walter, Schlaepfer, Rehme, Schmidt, and Keysers, (2009) found that reboxetine increased amygdala response bias specifically towards fear signals. In this study, compared to the placebo group, subjects in the reboxetine group showed increased amygdala activity to fearful pictures. Again other studies have, however, suggested that reboxetine might not increase processing of negative stimuli but selectively enhance processing of positive information, which would underpin its antidepressant effect (Harmer, Hill, Taylor, Cowen, & Goodwin, 2003; Harmer, Shelley, Cowen, & Goodwin, 2004; Norbury et al., 2008). The specific effect of reboxetine on emotional processing thus still remains unclear, as does the extent to which emotion processing might change over the course of reboxetine treatment. However, since, pharmacologically, a single dose of reboxetine enhances noradrenaline function, and since I have previously shown that a reduction in noradrenaline led to an increase in deontological moral judgments in personal moral dilemmas, the hypothesis was that reboxetine would lead to an increase in utilitarian moral decisions.

Method

Subjects

Subjects were recruited via poster and E-mail advertisement. They were first invited for an eligibility screening, which included a brief medical and psychological assessment to ensure that subjects were free of any axis 1 psychological disorder, as judged by a trained clinician using the Structured Clinical Interview for DSM-IV (SCID-IV) (Francis et al., 1995). Also subjects with any medical counter indication against reboxetine treatment were excluded. Subjects were 40 healthy individuals (M_{age} = 24.70, 20 male, 20 female). Subjects were paid in compensation for time and travel (£30).

Procedure

On a separate occasion after the screening subjects were invited for the study, which took place in the morning. Reboxetine or placebo was administrated in a random double blind manner, in a parallel group design, using sealed envelopes. Subjects were then free to relax, read, or work for 2 hours. The psychological tasks were administrated thereafter, which is in accordance with the peak plasma concentration of reboxetine (Gilman, 1996). Subjects` mood (happiness, sadness, aggression, alertness, tiredness, and anxiety) was assesssed at 3 time-points during the study (at baseline, just before drug/placebo administration; at + 120 min; and at + 200 min) using self-report Visual Analogue Scales (See Chapter 2). In addition subjects` heart rate was recorded every 30 min using a pulse oximeter.

Moral Dilemmas The moral dilemmas in this task were the same as those used in the previous propranolol study (see Chapter 2 and Appendix 2.3 for a detailed description). However, some additional moral dilemmas were added which involved less harmful acts then killing. These dilemmas were developed by Kahane et al. (2010) and were used to ascertain whether the previously observed effect would also be present if different, less serious, and probably more realistic scenarios, were chosen. Additionally, since I have discussed in the previous propranolol study that propranolol might have led to a reduction in concern for the consequences of the moral act, I also included 5 further moral dilemmas that varied in the severity of the consequences (i.e., 10 instead of 5 people were killed).

Finally, I have included 5 moral dilemmas that were specifically designed to be affected by changes in working memory capacity (i.e., those developed by Moore et al., 2008). The latter were included to further exclude the possibility that the effect observed

by noradrenergic blockade might be caused by changes in working memory capacity (see Appendix 4.1 for the full list of additional moral dilemmas included). All responses to moral dilemmas were given on two 5-point scales. The first question regarding moral acceptability was equivalent to the question in the previous propranolol study. I added a rating of confidence to this study. Subjects were asked to indicate how confident they were about the rating of moral acceptability (0 = *Not at all certain* and 5 = *completely certain*). This second question was included because it was demonstrated in the propranolol study that subjects were more decisive in their moral acceptability ratings in the propranolol group. Thus it might be expected that reboxetine would lead to an increase in uncertainty about the moral judgment.

Results

Physiological measure and self-reported mood

Heart rate differences were determined using two tailed student *t*-tests. I found that heart rate was significantly increased in the reboxetine group compared to the placebo group at 120min min and 150min post intervention, respectively ($M_{\text{placebo120min}}$ = 66.00, *SD* = 13.30; $M_{\text{reboxetine120min}}$ = 73.20, *SD* = 9.72, *t*(38) = -1.96, *p* = 0.06; $M_{\text{placebo150min}}$ = 65.90, *SD* = 10.19; $M_{\text{reboxetine150min}}$ = 74.10, *SD* = 11.17, *t*(38) = -2.43, *p* = 0.02) (See Figure 4.1.). There were no significant differences between the intervention groups in self-reported mood (all *ps* > .20).

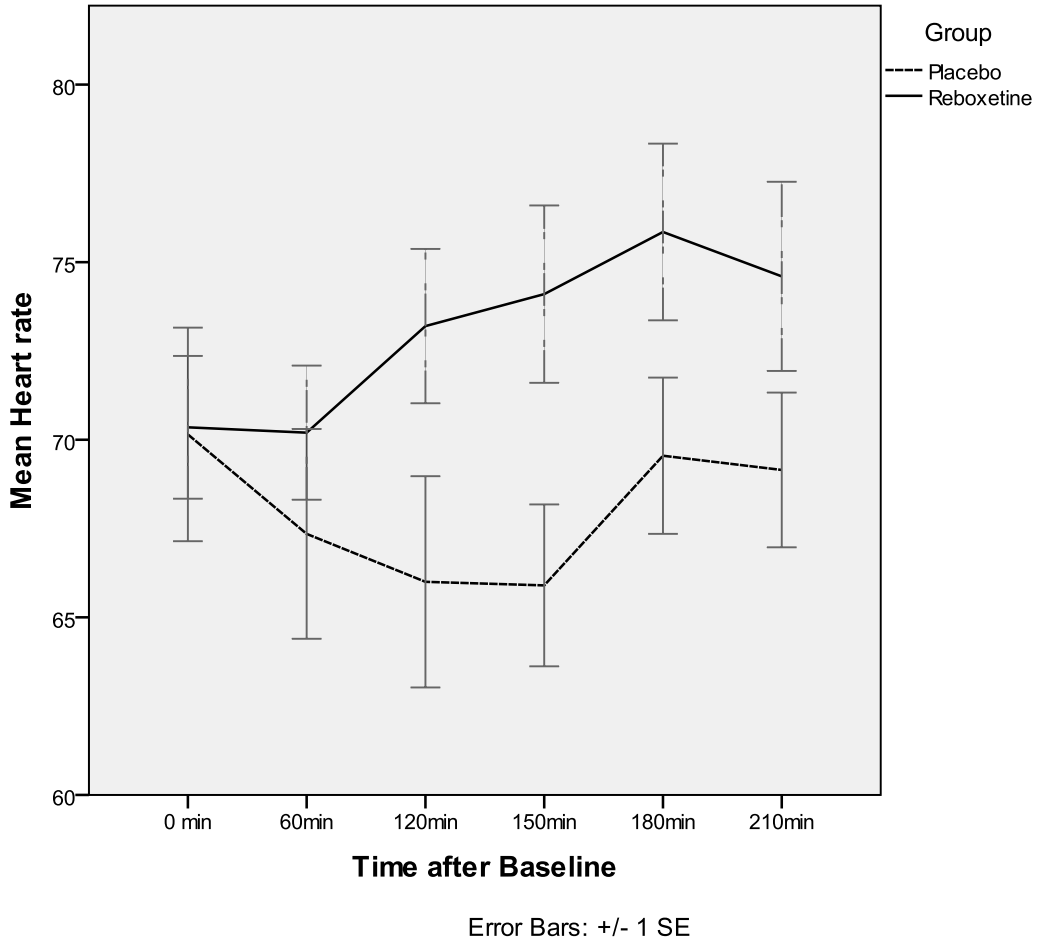


Figure 4.1 Heart rate changes in placebo and reboxetine group.

Moral Judgments

Theoretical moral dilemmas (Greene et al., 2001) To determine group differences in responses to the moral dilemmas, and to assess whether this effect was present depending on the moral question a 2 Intervention (placebo versus reboxetine) x 2 Dilemma type (personal versus impersonal) x 2 Question (moral acceptability versus certainty) mixed design ANOVA was computed with repeated measures on the last two factors. I found a significant main effect of Dilemma type ($F(1,38) = 20.31$, $p < .00$). Post hoc paired sample *t*-tests revealed that subjects rated personal moral dilemmas as less morally acceptable ($M = 2.92$, $SD = .72$) then impersonal moral dilemmas ($M = 3.71$, $SD = .72$) ($t(39) = 8.11$, $p < .00$). In addition, I found a main effect of Question ($F(1,38) = 101.87$, $p < .00$). For both personal and impersonal moral dilemmas, the moral acceptability question was rated higher ($M = 3.71$, $SD = .72$; $M = 2.91$, $SD = .72$) than the question about certainty of the answer ($M = 1.54$, $SD = .31$, $M = 1.89$, $SD = .35$) ($t(39) = 16.40$, $p< .00$; $t(39) = 7.30$, $p< .00$). Also, I found a significant interaction of dilemma-type and question ($F(1,38) = 13.19$, $p < .00$). The question of moral acceptability was more positive in impersonal ($M = 3.71$, $SD = .72$) then in personal dilemmas ($M = 2.92$, $SD = .72$) ($t(39) = 8.11$, $p < .00$), whilst the question of certainty had higher means in personal moral dilemmas ($M = 1.89$, $SD = .35$) compared to impersonal ($M = 1.54$, $SD = .31$) ($t(39) = -9.72$, $p < .00$) (see Table 4.).

	Dilemma type	
Question	Impersonal	Personal
Acceptability	*M* = 3.71	*M* = 2.91
	SD = .72	*SD* = .72
Certainty	*M* = 1.54	*M* = 1.89
	SD = .31	*SD* = .35

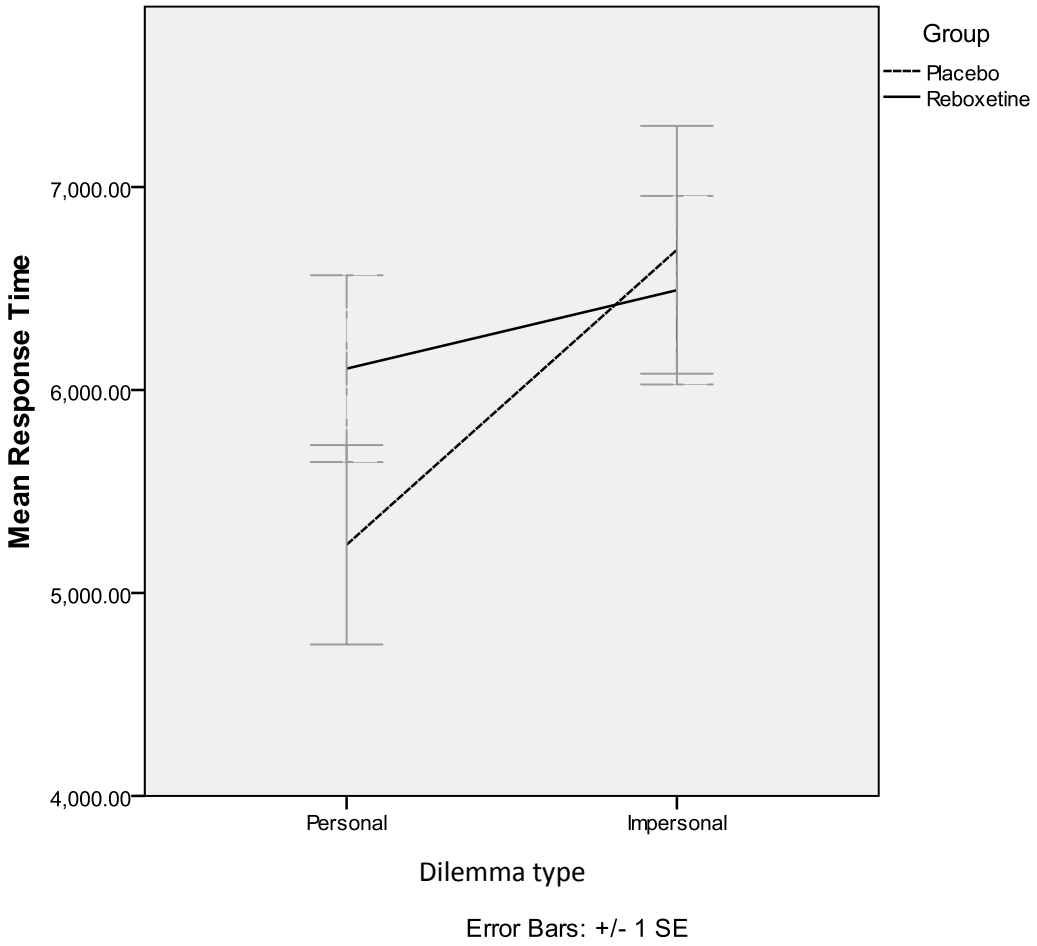
Table 4.1 Question and Dilemma type differences in rating.

However, there were no group effects of placebo versus reboxetine, nor any significant interaction effects of the factor Intervention (all *ps* > .20).

Response time To determine differences between reboxetine and placebo group in response times to the moral dilemmas a 2 Intervention (placebo versus reboxetine) x 2 Dilemma type (personal versus impersonal) x 2 Question (moral acceptability versus certainty) mixed design ANOVA was computed with repeated measures on the last two factors. One subject from the placebo group was excluded from this analysis, because of excessively slow responding. A significant main effect of Dilemma type was found ($F(1,37) = 7.11$, $p = .01$). Subjects answered faster to both questions in impersonal compared to personal moral dilemmas ($M_{acceptability/impersonal}$ = 5682.38, *SD* = 2117.41; $M_{acceptability/personal}$ = 6588.71, *SD* = 2349.99) ($M_{certainty/impersonal}$ = 1712.21, *SD* = 603.09; $M_{certainty/personal}$ = 1813.55, *SD* = 420.23) ($t(38) = -2.64$, $p = .01$). Additionally, I found a main effect of question ($F(1,37) = 7.44$, $p < .00$). Response times to the certainty question were higher than those to the moral acceptability question in impersonal and personal moral dilemmas (*M* = 5682.38, *SD* = 2117.41; *M* = 1712.21, *SD* = 603.09) (*M* = 6588.71, *SD* = 2349.99; *M* = 1813.55, *SD* = 420.23) ($t(38) = 12.99$, $p< .00$; $t(38) = 13.79$, $p < .00$). However, no significant main or interaction effects were found for Intervention. As depicted in Figure 4.2 there was a slight, non-significant, trend for subjects to respond

more slowly to the moral acceptability question in personal, but not impersonal moral dilemmas.

Figure 4.2 Response time differences in reboxetine and placebo group for personal and impersonal moral dilemmas.



Theoretical moral dilemmas involving lying A two tailed *t*-test was computed to determine differences in responses to moral dilemmas involving lying. Responses were determined by calculating the average response to the 5 moral dilemmas. Means were log transformed to achieve normally distributed scales, as determined with the Kolmogoroff-Smirnhoff test. There was a non-significant trend for subjects in the reboxetine group to regard actions in moral dilemmas involving lying as more morally acceptable then did subjects in the placebo group ($t(38) = 1.37$, $p = .18$) (see Figure 4.3).

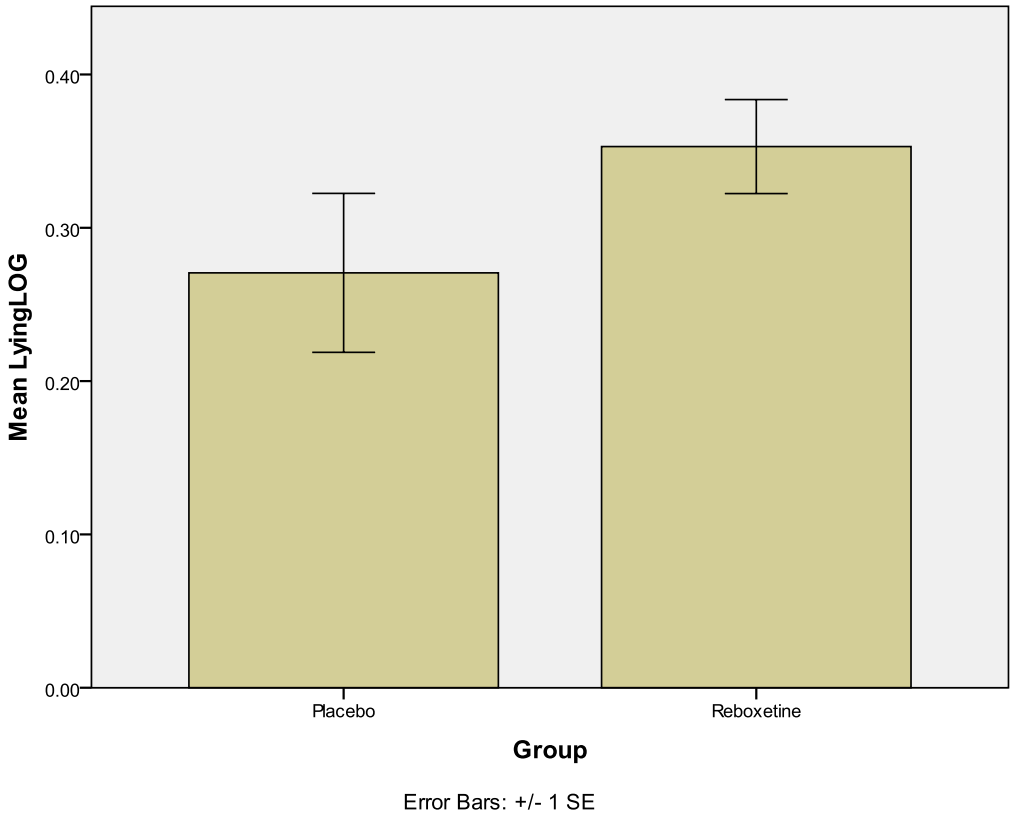


Figure 4.3 Mean acceptability ratings to moral dilemmas involving lying for placebo and reboxetine group. Note. Non-normally distributed data were Log transformed.

Further moral dilemmas There were no differences between the placebo and reboxetine groups for either moral dilemmas involving more severe outcomes, or moral dilemmas based on Moore et al. (2006) (all *ps* > .20).

Discussion

This study investigated the effect of noradrenergic enhancement on moral judgments. Reboxetine significantly increased subjects' heart rate but did not lead to changes in responses to theoretical moral dilemmas. I found that, regardless of intervention, all subjects rated personal moral dilemmas as less morally acceptable than impersonal dilemmas. Additionally, all subjects were more certain about their judgment and had reduced response times in impersonal compared to personal dilemmas. This is in accordance with the answer pattern commonly found for theoretical moral dilemmas, and supports the idea that indeed impersonal and personal dilemmas might be processed differently (e.g., Greene et al., 2001).

This study tested the hypothesis that subjects in the reboxetine group would rate actions in personal moral dilemmas as more morally acceptable. However, there were no significant differences in moral acceptability ratings for the reboxetine and placebo group. There was a trend for subjects in the reboxetine group to rate actions in moral dilemmas involving lying as more morally acceptable, and they also responded slightly faster to personal but not impersonal moral dilemmas. My hypothesis was based on the previous study demonstrating that noradrenergic blockade led to an increase in deontological moral judgments. There is indeed some evidence that noradrenergic enhancement might have opposite behavioural effects than noradrenergic blockade (de Martino et al., 2008; Onur et al., 2009). However, the evidence for this is still quite mixed. For example, some studies

did not find any behavioural differences after a single dose of reboxetine in emotional tasks (O'Carroll & Papps, 2003). Also whereas reboxetine would stimulate both, alpha- and beta post-synaptic receptors, propranolol would specifically lower activity at post-synaptic beta receptors. It may be that simultaneous activation of both alpha and beta receptors obscures an effect of beta receptor stimulation to modify moral judgements. Also, it might be speculated that experimental pharmacological enhancement might lead to pharmacological ceiling effects.

Another explanation for the results might be that reboxetine intervention did not lead to an increase in negative emotional arousal (such as fear) but, rather, to an increase in positive emotional processing (in accordance with its later antidepressant effect). For example, Norbury et al. (2008) found that longer term (7 days) administration of reboxetine led to greater activation to positive relative to negative words in left precuneus and right inferior frontal gyrus during an emotional word categorisation task and reduced responses in left precuneus, anterior cingulated, and medial frontalgyrus during a recognition task. Also Harmer et al. (2004) found that 7 day treatment with reboxetine as well as a single dose of reboxetine (Harmer et al., 2003) enhanced the speed of categorising positive versus negative personality characteristic words in healthy volunteers. Additionally Harmer et al. (2004) and Harmer et al. (2003) found that reboxetine also led to increased free recall of positive compared to negative personality characteristic words. Thus Norbury et al. (2008) concluded that reboxetine was associated with increased salience of positive words. This would support the suggestion that reboxetine might not have led to an increase in emotional arousal that was opposite to the effect observed by propranolol. Propranolol is consistently used for treatment of acute anxiety and its anxiolytic effect is thus well documented (e.g., Chamberlain et al., 2004). Thus, even though both drugs affect noradrenergic transmission the resulting effect on emotion

processing might not be opposite, and both drugs might have positive effects on emotional processing but in different ways. This would then also suggest that the effect of an increase in deontological moral judgment with propranlol might be specific to a reduction in anxiety, and not to general emotional blurring. Reboxetine, on the other hand, might not have led to a similar increase in all noradrenergic emotional responses, for example fear (i.e., fight and flight responses), that were targeted by propranolol, and thus might not have produced the anticipated effects on moral judgements. Further research might utilise other means of increasing anxiety – such as experimental mood manipulations – and determine if this would then lead to an increase in utilitarian moral judgments.

It might, however, be of considerable practical importance that this study found that reboxetine, which is a widely used antidepressant medication, did not seem to affect individuals' theoretical moral decision making. For example, judgments made in court cases (e.g., by members of the jury) might have been affected if made under the influence of noradrenergic based antidepressant medication.

Study 4 Reboxetine effect on implicit and explicit racial attitudes

Introduction

Automatic emotional arousal might be causally relevant for implicit racial prejudice. I found that propranolol reduced implicit but not explicit negative racial associations (See Chapter 3). This finding suggests that noradrenergic mediated arousal might play a causal role in implicit racial attitudes. Propranolol has been shown to reduce noradrenergic transmission and also to reduce processing of emotional stimuli (e.g, Chamberlaine et al., 2004). For example, Van Stegeren et al. (2005) found that propranolol reduced amygdala activity to emotional pictures, and numerous studies have demonstrated its effect on reducing emotional arousal associated with traumatic memories (see Chamberlain et al, 2004, for a review). To further investigate the causal role of noradrenergic mediated emotional arousal in implicit racial attitudes I thus also researched the effect of reboxetine on racial prejudice. If noradrenergic mediated arousal plays a causal role in implicit negative racial attitudes then a noradrenergic enhancing agent should increase implicit but not explicit racial bias.

Method

Subjects

The 40 subjects from reboxetine study 1 also completed the measures of racial attitudes. The IAT was administrated 150 min after reboxetine or placebo intervention and the explicit prejudice measure was completed after the IAT.

Procedure

Implicit racial associations For a description of the IAT please see Chapter 3. The racial IAT used in this reboxetine study was the same as the one previously used in the propranolol study.

Explicit racial prejudice In addition to the feeling thermometer, which I also used in the propranolol study (see Chapter 3), I added a second method to measure explicit racial bias. In the second explicit measure subjects rated their feelings towards black and white people on six 8-point semantic-differential items (for placebo group [alpha] = .87; for reboxetine group [alpha] = .92): 1. 0 = *cold*, 7 = *warm*; 2. 0 = *positive*, 7 = *negative;* 3. 0 = *hostile*, 7 = *friendly*; 4. 0 = *trusting*, 7 = *suspicious*; 5. 0 = *contempt*, 7 = *respect;* 6. 0 = *disgust*, 7 = *admiration.* (7). The items were coded so that a higher score indicated a more positive outgroup evaluation; items 2 and 4 were coded reverse. This method for assessing explicit prejudice towards other groups was based on previous research, for example by Wright, Aron, McLaughlin-Volpe, and Ropp (1997). I included this second measure of explicit prejudice to ensure that the absence of an effect of propranolol on explicit prejudice in Chapter 3 was not reliant on only one specific test of explicit prejudice (See Appendix 4.2 for the questionnaire).

Results

Physiological measures and self-reported mood As reported in reboxetine study 1, reboxetine significantly increased heart rate, but did not lead to changes in self-reported mood.

Explicit racial prejudice For the semantic differential measure a two-tailed student *t*-test revealed no significant difference between conditions for either the total score including all emotions or for each emotion separately (all *ps* > .20). In addition a non-parametric Mann Whitney U-test demonstrated that there were also no differences between explicit racial prejudice in reboxetine and placebo groups on the feeling thermometer ($p > .20$).

Racial implicit association test The IAT was analysed according to the standard algorithm as provided by Greenwald et al. (1998)[4]. Trials were first inspected to eliminate extreme values (i.e., those with response times lower than 300 ms or higher than 4000 ms). Subsequently, to determine the IAT effect, the mean response time for congruent trials was subtracted from the mean response time for incongruent trials. Mean scores were log transformed before subtraction. In addition outliers (i.e., those who respond excessively slowly (< 3000 ms) and those who made numerous errors (< 20 %)) were detected. Two subjects (1 from the reboxetine and 1 from placebo group) were excluded because they responded excessively slowly on all congruent trials. In addition one further subject from the reboxetine group was excluded from further analysis because of numerous errors across all blocks. First, a Student's *t*-test was performed on the IAT score and revealed no significant differences between placebo ($M = .08$, $SD = .08$) and reboxetine ($M = .09$, $SD = .07$) ($t(34) = .57$, $p = .56$) groups. Second, I computed a 2 Congruency (congruent versus

[4]Note that the IAT in this study was not analysed with the more complex method (the improved algorithm) since the standard method did not reveal a positive – or near positive - result. Differences between the two analysis methods do not lead to gross changes in statistical significance.

incongruent) x 2 Intervention (placebo versus reboxetine) mixed ANOVA, with repeated measures on the first factor. There was a main effect of Congruency ($F(34,1) = 42.11$, $p < .00$). Post hoc paired sample *t*-tests revealed that the response time for congruent trials ($M = 599.97$, $SD = 73.82$) was significantly smaller than the response time for incongruent trials ($M = 733.39$, $SD = 137.16$) ($t(35) = -6.52$, $p < .00$). However, the interaction of congruency and intervention was not significant ($F(34,1) = .39$, $p = .54$). As shown in Figure 4.5, there was a slight, non-significant, trend for reboxetine to increase response times for incongruent trials, but it did not reduce response times for congruent trials.

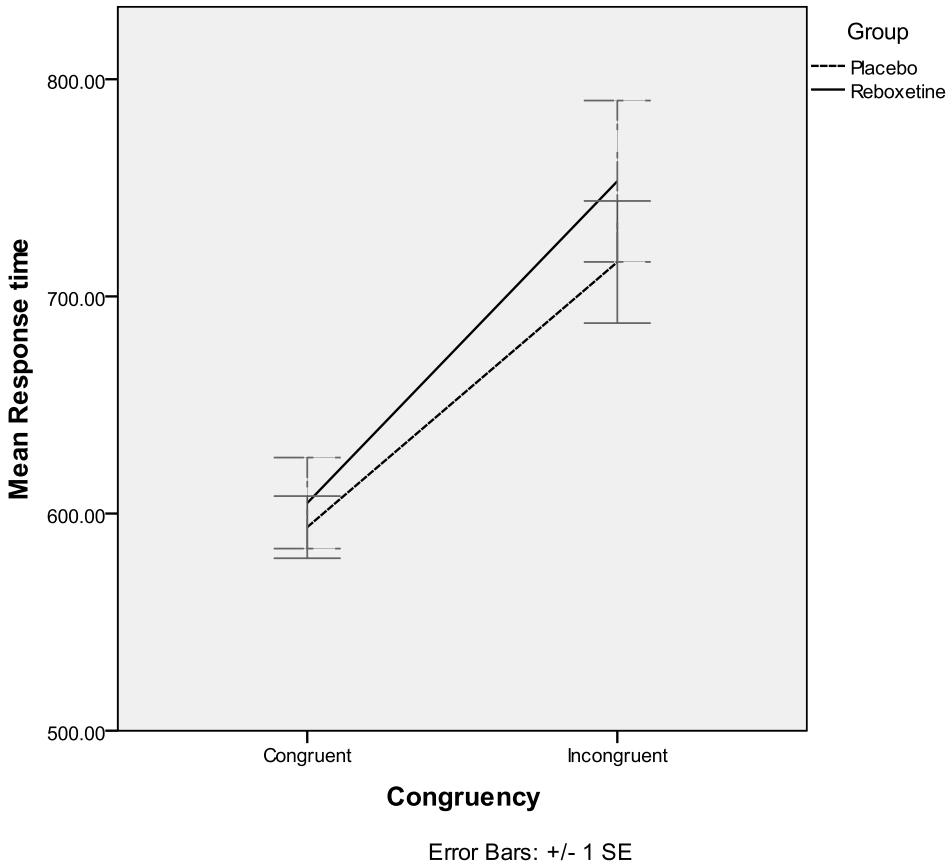


Figure 4.4 Mean response times on congruent and incongruent IAT trials in placebo and reboxetine groups.

Discussion

This study investigated the effect of a single dose of reboxetine on implicit and explicit racial attitudes. Contrary to predictions, there was not an effect of reboxetine on implicit racial associations. The IAT effect is determined by subtracting the congruent from the incongruent condition. Negative implicit associations can be interpreted as the response time difference between congruent and incongruent trials. A high IAT score reflects a greater response time for incongruent compared to congruent trials. In research reported earlier in this thesis, on the effect of propranolol on the IAT (Chapter 3, Terbeck, Kahane, McTavish, Savulescu, Cowen, Hewstone, 2012), I found that propranolol diminished racial bias. Specifically subjects in the propranolol group were slightly faster on incongruent and slower on congruent trials. Thus, the total IAT score was significantly smaller. In order for the IAT score to be significantly higher, I predicted that in the reboxetine condition response times would increase for congruent trials and decrease for incongruent trials. As predicted, I indeed found a trend for reboxetine to increase response times for incongruent trials, but it did not seem to affect response speed to congruent trials. It might be suggested that subjects were already at the maximum speed of responding in the case of congruent trials and thus that a ceiling effect was present. This would suggest that reboxetine might have had the effect of increasing implicit racial prejudice, as predicted, but that the IAT was unable to determine this. Further research might use behavioural methods, such as testing changes in interaction with out-group members, to determine whether there had been an increase in implicit bias.

Another explanation is that reboxetine did indeed not affect implicit attitudes. Research has suggested that reboxetine might also enhance positive emotional processing (Harmer et al., 2003; Harmer et al., 2004; Norbury et al., 2008) rather than just simply

increasing fear responses. As with the possible explanation for the effect of reboxetine on moral judgments, affective arousal, such as fear responses, that were specifically targeted by propranolol might have determined the previous effect. Also, as noted above, pharmacologically reboxetine is not a "mirror image" of propranolol and so their psychological effects may not be opposite. An opposite pharmacological effect to that of propranolol would be produced by a beta receptor agonist (acting at both beta 1 and beta 2 receptors). However, there are no agents of this nature available for use in humans that readily cross the blood brain barrier (Gilman, 1996).

General Discussion

These two studies examined the effect of reboxetine on moral and social judgments. Even though reboxetine led to a significant increase in heart rate it did not have an effect on theoretical moral judgments or implicit/explicit racial attitudes. This demonstrates that antidepressant medication based on noradrenergic reuptake inhibition does not affect moral or social judgments. Since I found that noradrenergic blockade did, however, change moral judgments and implicit attitudes (see Chapters 2 and 3) it might be speculated that the noradrenaline enhancing effect of reboxetine did not have linear effects on emotion processing compared to noradrenergic blockade via propranolol. Indeed previous research has also demonstrated that whilst propranolol leads to a reduction in emotional arousal such as fear responses (e.g. Chamberlain et al., 2004), reboxetine does not necessarily lead to an increase in fear (Bruel, Kaffenberger, & Herwig, 2010), but rather to in increase in positive emotional processing (Harmer et al., 2003; Harmer et al., 2004; Norbury et al., 2008). This research thus also demonstrates that drugs with pharmacological effects that are in some ways pharmacologically opposite do not necessarily lead to opposite behavioural effects. Further research might thus determine the precise behavioural and pharmacological effects by comparing blocking and enhancing agents.

Further, it may be that the dose of reboxetine used in this research was too low. However, acute use of this dose was shown to significantly increase heart rate, and also produced positive effects on emotional processing in another study (Harmer et al., 2004). Thus it seems sufficient to produce noradrenergic mediated activation and relevant neuropsychological changes.

In conclusion, noradrenergic enhancement via reboxetine was found not to affect moral and social judgments. It is suggested that pharmacological enhancement is not the "mirror image" to pharmacological blockade and thus that different emotional responses might have been targeted. Most probable, propranolol led to reduced negative emotional arousal, and the antidepressant reboxetine to increased positive emotional arousal. Following this, negative emotional arousal seems more relevant for moral and social judgments.

CHAPTER 5: EFFECT OF β-ADREMOCEPTOR BLOCKADE ON THE NEURAL RESPONSES TO OUTGROUP FACES

Introduction

The role of emotion in implicit racial associations has been demonstrated by recent research, which has also implicated the amygdala as a key brain region in such implicit emotional responses (Cunningham et al., 2004; Phelps et al., 2000; Stanley et al., 2008). In line with this work, I also found that a single dose of the β-adrenoceptor antagonist, propranolol, significantly reduced implicit racial bias measured by IAT, but not explicit prejudice (see Chapter 3). This result suggests that noradrenergic-mediated arousal, which is sensitive to propranolol, may play a causal role in some forms of implicit racial bias. I speculated that the reduction in implicit bias may have been associated with a modulation of central noradrenergic transmission in limbic and other brain areas that have previously been found to be activated by presentation of outgroup stimuli. These areas include a network of limbic, and cortical regions, including the amygdala, insula, fusiform gyrus, anterior cingulate cortex, and dorsolateral prefrontal cortex (Cunningham et al., 2004; Knutson et al., 2007; Phelps et al., 2000; Richeson et al., 2003; Stanley et al., 2008).

The aim of the present study was to investigate the effect of propranolol on the neural response to outgroup versus ingroup faces, specifically the viewing by white people of unfamiliar black versus white faces. A previous study has shown that viewing unfamiliar (Study 1) but not familiar (Study 2) black compared to white faces was associated with amygdala activation that correlated with implicit racial bias (Phelps et al., 2000). I therefore predicted that propranolol would decrease amygdala activation to black versus white faces, and that activity in the amygdala to this presentation would correlate with IAT scores.

Method

Subjects

Thirty right handed healthy individuals (M_{age} = 24.10 years; 14 male, 16 female) participated in this research after written informed consent was obtained. Subjects were recruited via poster and e-mail advertisements and were initially medically and psychologically screened, including measurement of blood pressure and the recording of a normal ECG (See Appendix 2.1 for the Case Record Form of study 1 and 2, which used a similar procedure). Subjects with any contra-indications to propranolol administration, MRI scan, as well as any history of mental illness, as assessed by the Structural Clinical Interview for DSM-Clinical Version, SCID-IV (Francis et al., 1995), Beck`s Depression Inventory (Beck, Ward, Mendelson, Mock, & Erbaugh, 1961), as well as Eysenck`s Neuroticism and Psychoticism scale (Eysenck, & Eysenck, 1964), were excluded from the study. The study was approved by the Oxford NHS research ethics committee.

Procedure

The study used a double-blind, placebo-controlled, parallel group design where subjects were randomly allocated to receive either placebo or propranolol (40 mg) orally, one hour before functional magnetic resonance imaging (fMRI), to achieve a peak plasma concentration of propranolol (Gilman, 1996) during the scan. Subjects were scanned for 30 minutes and tests of implicit and explicit prejudice were then completed outside the scanner.

fMRI task

The design of the fMRI task was based on Phelps et al. (2000). Subjects viewed unfamiliar black and white male faces in the scanner. The faces were taken from the Stanford University faces database. These faces were previously rated, by over 100 subjects in an online web study from Stanford University, on the dimensions of attractiveness, stereotypicality, and age. Attractiveness and stereotypicality dimensions were rated using a 7-point scale, while the age dimension used a 10-point scale. I selected a group of 36 black and white faces each that did not significantly differ on the ratings of attractiveness, stereotypicality, and age. In the fMRI task, nine 18-second blocks of a baseline fixation cross (condition A) were interleaved with eight 18-second blocks consisting of four blocks of white faces (condition B) and four blocks of black faces (condition C). During each task block subjects viewed 9 faces, each presented for 1500 ms, and subjects were asked to judge the age of the person in the picture (*Is the person older than 25 years?* 0 = *No* or 1 = *Yes*), which was analogous to the procedure used by Wheeler and Fiske (2005). Stimuli were presented using E-Prime (Version 1.0) and a cloned projection displayed to subjects on an opaque screen located at the head of the scanner bore, which subjects viewed using angled mirrors. Subjects responded via an MRI-compatible keypad. Stimulus presentation/subject button presses were registered and time-locked to fMRI data using E-Prime. Both accuracy (correct judgement of age) and reaction times were recorded for 1000 ms, and 500 ms inter-stimulus intervals. Four blocks of resting – staring at the central fixation cross – were interleaved and lasted for 18000 ms each. Faces were presented in random order.

fMRI data acquisition All imaging data were obtained using a 3T Siemens Tim Trio system located at the Oxford Centre for Clinical Magnetic Resonance Research (OCMR). Functional imaging consisted of T_2*-weighted echo-planar image (EPI) slices (repetition

time (TR) = 2000 ms, echo time (TE) = 28 ms, matrix = 192 x 192), 3.5mm slice thickness. The first two EPI volumes in each session were discarded to avoid T1 equilibration effects.

fMRI data analysis Functional MRI data were pre-processed and analysed using FSL (Version 4.8, www.fmrib.ox.ac.uk/fsl). Pre-processing included slice acquisition time correction (using Fourier-space time-series phase-shifting), within-subject image realignment, non-brain removal spatial normalization to a standard template (Montreal Neurological Institute, MNI, 152 stereotactic template), using an affine procedure and spatial smoothing using a Gaussian kernel (5 mm full-width-half-maximum). The time series in each session was high-pass filtered (to a maximum of 0.0125-Hz). Analyses of data from individual subjects were computed using the general linear model approach with local autocorrelation correction. For the faces task the two explanatory variables were modelled: 'black', 'white' and 'fixation'. In addition, temporal derivatives were included in the model as covariates of no interest to increase statistical sensitivity. All variables were modelled by convolving each block with a haemodynamic response function, using a variant of a gamma function (that is, a normalization of the probability density function of the gamma function) with a standard deviation of 3 s and a mean lag of 6 s. At the group level, data were analysed using a mixed effects analyses. In a whole brain analysis, significant activations were identified using cluster-based thresholding of statistical images with a height threshold of Z = 2.5 and a (corrected) spatial extent threshold of $p < 0.05$. In addition to our whole brain analysis I also examined left and right amygdala as *a priori* regions of interest, which were determined with an anatomical mask taken from the Harvard-Oxford sub-cortical atlas (http://fsl.fmrib.ox.ac.uk/fsl/fslwiki/Atlases).

Behavioural Tasks

Implicit Association Test The Implicit Association Test (IAT) (Greenwald et al., 1998) was employed using E-prime (Version 2.0) software (see Chapter 3 for a detailed description of the task). The faces for the IAT task were not the same faces as used in the fMRI task.

Explicit prejudice Explicit prejudice was measured using two different methods;

a) The feeling thermometer (Converse & Presser, 1986) (see Chapter 3 for a detailed description of the questionnaire).

b) A six 8-point semantic-differential (See Chapter 4 for a detailed description)

Self-reported Mood: Visual analogue scales Self-reported mood was assessed using visual analogue scales (see Chapter 2 for a detailed description).

Results

Demographic data, heart rate change

Both groups were well matched across all demographics measured, including depression and personality scores (see Table 5.1).

Table 5.1

Demographic variables for Propranolol and Placebo group

Variable	**Group**		**Significance**
	Propranolol	**Placebo**	
Age	*M* = 20.07 *SD* = 1.16	*M* = 21.53 SD = 2.64	ns.
Body Mass Index (BMI)	*M* = 22.66 *SD* = 2.13	*M* = 23.24 *SD* = 2.90	ns.
Beck Depression Inventory (BDI)	*M* = 1.43 *SD* = 1.70	*M* = 1.07 *SD* = 1.16	ns.
Eysenck Neuroticism scale	*M* = 2.36 *SD* = 2.13	*M* = 1.27 *SD* = 1.62	ns.
Eysenck Psychoticism scale	*M* = 2.21 *SD* = 1.12	*M* = 2.60 *SD* = 1.72	ns.

Note. ns. = non-significant on $p > .05$

Heart rate analysis I computed a 2 (Intervention: placebo versus propranolol) x 6 (Time) mixed repeated measures analysis of variance (ANOVA) with repeated measures on the latter factor. A significant Intervention x Time interaction was found ($F(5,24) = 5.21$, $p < .00$). Heart rate was significantly reduced in the propranolol group 30 min after treatment and remained lower for all further 30 min measurement points (at 0 min: propranolol (PR): $M = 69.20$, $SD = 10.85$, placebo (PL): $M = 73.53$, SD: 9.42; $t(28) = -1.17$, $p = .25$; at 30 min: PR: $M = 65.87$, $SD = 10.63$, PL: $M = 73.07$, $SD = 7.53$; $t(28) = -2.14$, $p = .04$; at 60 min: PR: $M = 59.93$, $SD = 10.22$, PL: $M = 72.33$, $SD = 9.46$; $t(28) = -3.45$, $p < .00$; at 90 min**:** PR: $M = 55.33$, $SD = 9.36$, PL: $M = 69.27$, $SD = 7.23$; $t(28) = -4.56$, $p < .00$; at 120 min**:** PR: $M = 56.67$, $SD = 8.84$, PL: $M = 70.93$, $SD = 8.92$; $t(28) = -4.4$, $p < .00$; at 150 min**:** PR: $M = 57.47$, $SD = 8.22$, PL: $M = 70.07$, $SD = 6.38$; $t(28) = -4.69$, $p < .00$) (see Figure 5.1).

Figure 5.1 heart rate in intervention groups

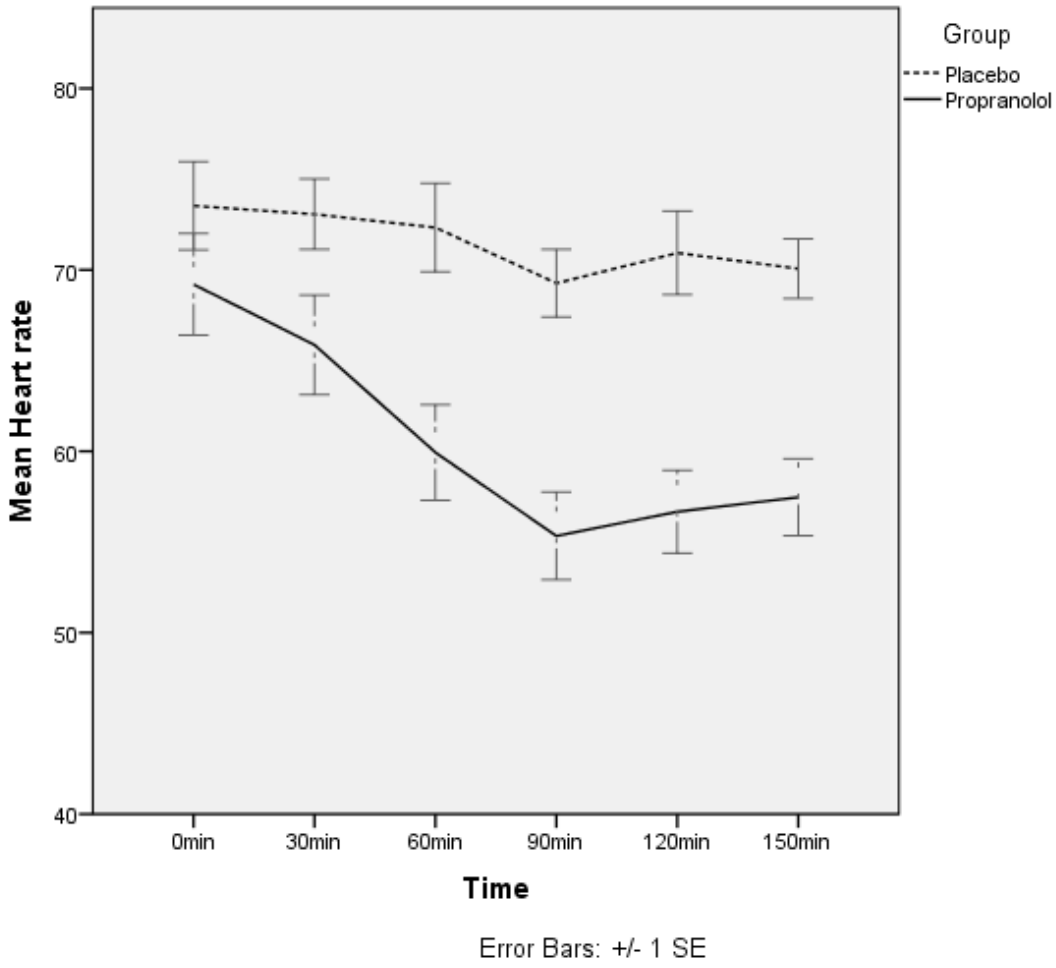


Figure 5.1. Heart rate changes over time (in min) in placebo and propranolol group.

Self-reported mood There were no group differences in self-reported mood at any of the 3 measurement times (all *ps* > .2).

Behavioural Tasks

Implicit Association Test The IAT was analysed according to the Greenwald et al., (2003) improved algorithm. Due to a technical failure data for one subject in the placebo group was not recorded. In the analysis all trials (main and practice) were considered. Following the procedures of the improved algorithm, errors were replaced with the mean for correct trials in that block + 600 ms. The resulting values were divided by their pooled standard deviation for correct trials (for a full description of the method see Chapter 3, and Greenwald et al., 2003). Three subjects had excessive error rates as well as more than three consecutive errors in the main blocks and were thus excluded. In addition the practice trials of two subjects were not included in the main analysis as they were excessively slow in responding (i.e., response times over 4000 ms). The corrected difference between congruent and incongruent trials revealed the standardized IAT effect. While the IAT was numerically lower in the propranolol treated subjects (M = .42, SD = .41) compared to the placebo group (M = .85, SD = .80), the difference was not significant ($t(24) = -1.60$, p = 0.11, d = .68) (see also Figure 5.2) although a clear trend was apparent (p one tailed = .056). Power analysis (*Power* = .8, p = .05) revealed that a minimum sample size of 28 per group would be required for this effect to be significant (see Figure 5.2).

Figure 5.2 IAT score in Placebo and Propranolol group.

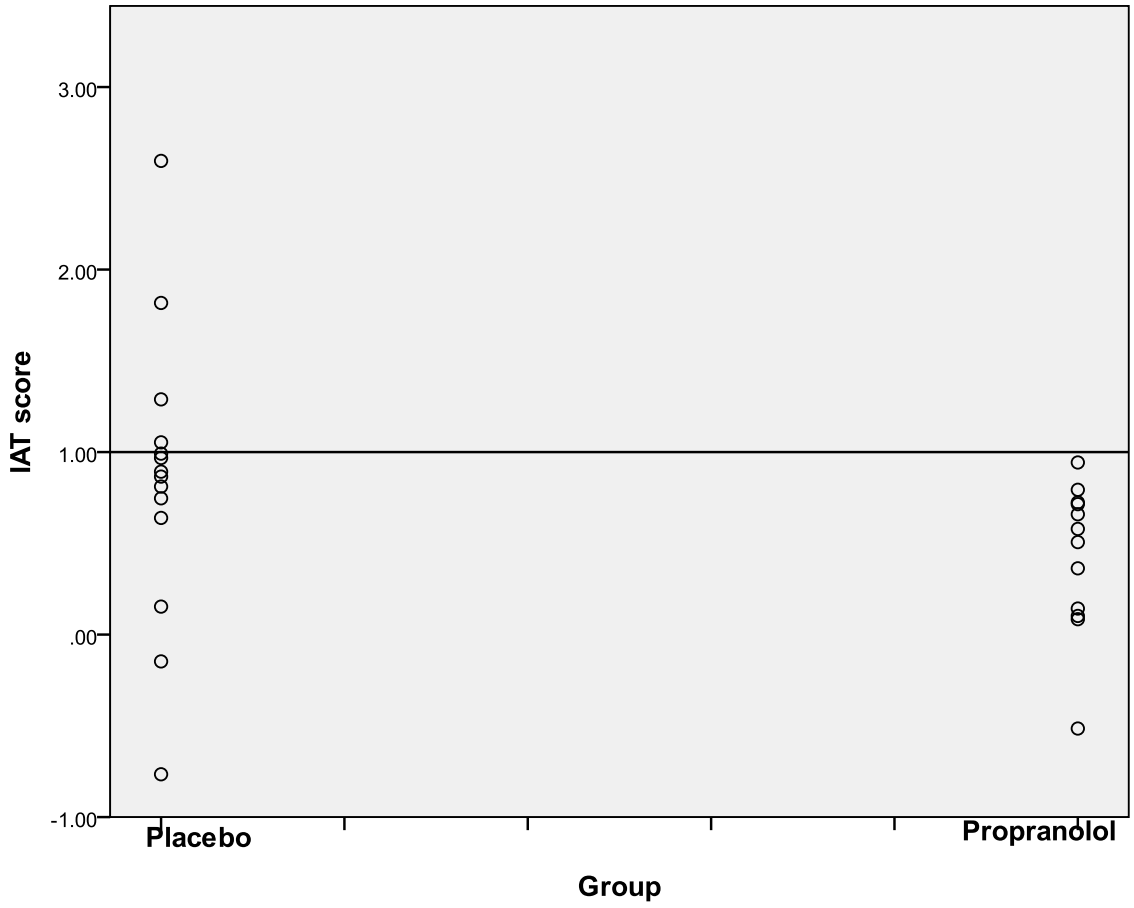


Figure 5.2 IAT score in Placebo and Propranolol group. *Note.* Scores are normalised by division trough the pooled standard deviation for correct trials, as stated in the improved algorithm analysis.

Explicit prejudice I first computed a Student's *t*-test to determine group differences in self-reported feelings towards black people on the semantic differential measure based on (Wright et al., 1997). There were no significant differences between propranolol and placebo conditions in explicit prejudice (PR: M = 32.67, SD = 6.59; PL: M = 30.93, SD = 6.59; $t(27) = -.71$, $p = .49$). For the non-normally distributed second measure of explicit prejudice – the feeling thermometer – I conducted a Mann-Whitney U-test to determine group differences; again there were no significant differences in explicit racial prejudice ($p > .2$). A one-tailed non-parametric correlation revealed that the two measures of explicit prejudice were significantly positively correlated (Spearman`s $R = .34$, $p = .04$).

Behavioural measures/ fMRI task A 2 Intervention (propranolol versus placebo) x 2 Race (black versus white) mixed ANOVA revealed a significant main effect of Race on response time ($F(1,25) = 15.50$, $p < .01$). Post hoc paired *t*-tests revealed that subjects' response time for the age judgments was higher for white (M = 841.02, SD = 192.02) compared to black (M = 773.56, SD = 201.09) ($t(26) = -3.83$, $p < .01$) faces. Importantly, however, the ANOVA revealed no interaction effect with treatment ($p > .05$).

Additionally, I evaluated differences in the age judgments (i.e., older or younger than 25 years). First the total number of "older" and "younger" judgments was calculated for each race separately (i.e., how many times subjects rated a person to be younger than 25, and how many times subjects rated a person to be older than 25). A paired *t*-test revealed that generally pictures of black people were significantly less rated as being younger than 25 years (M = 27.19, SD = 8.07) compared to pictures of white individuals (M = 34.23, SD = 6.25) ($t(25) = -3.67$, $p < .01$). Importantly, however, there were no effects of treatment.

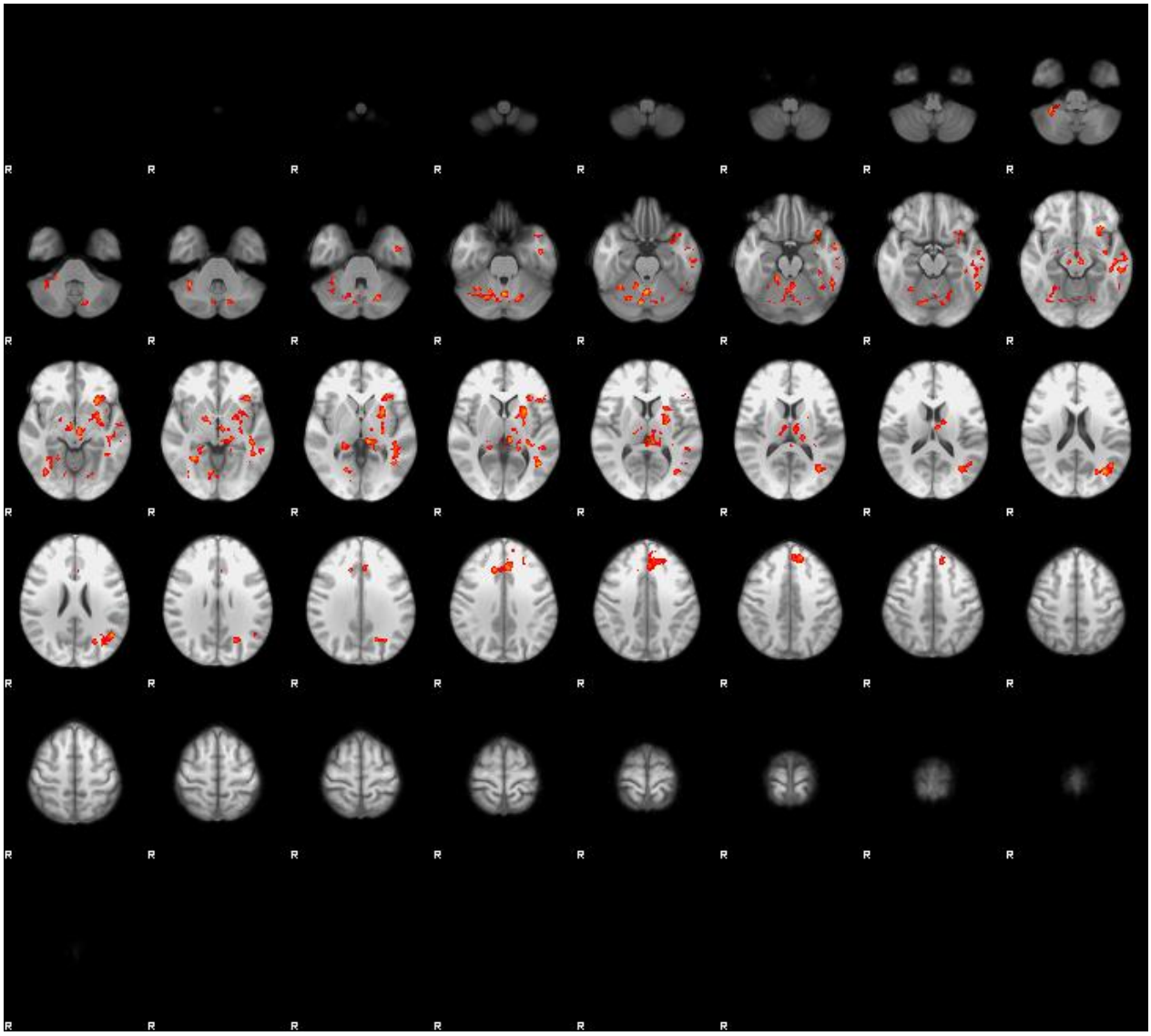
Neural responses

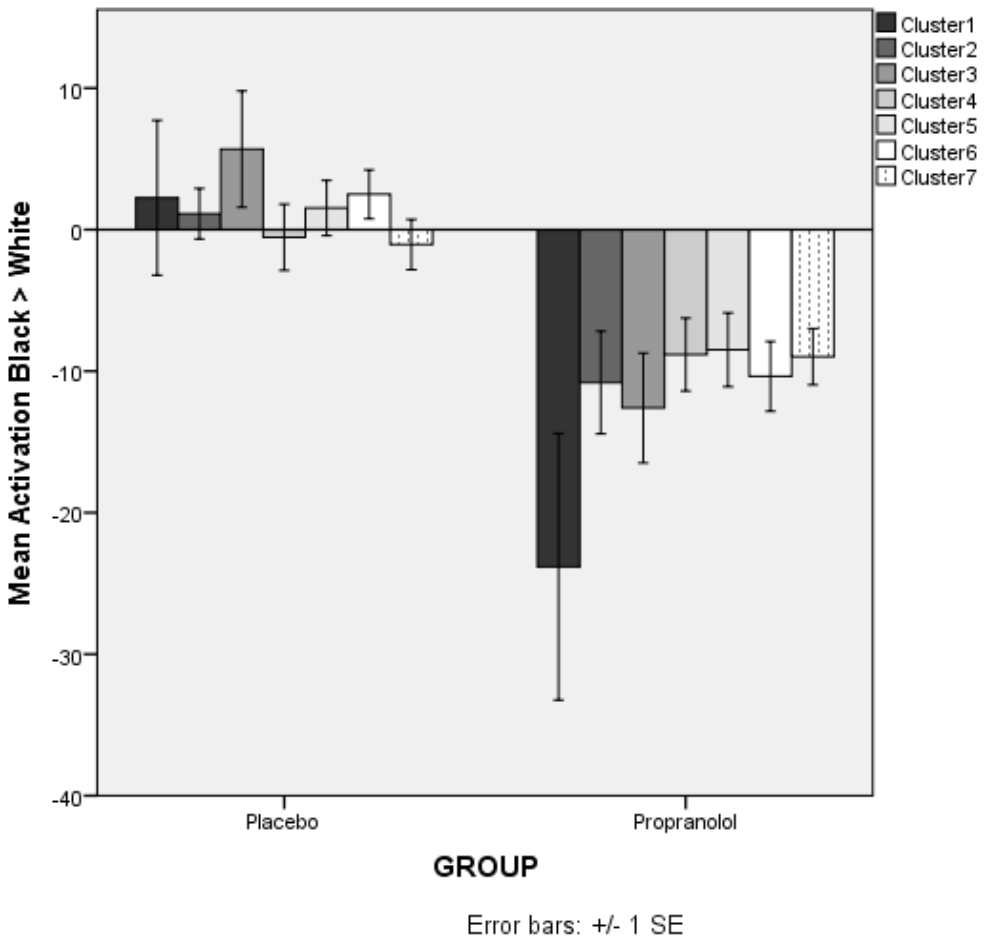
Whole brain analyses revealed greater activation under placebo versus propranolol for black versus white faces in right dorsolateral prefrontal, left cingulate, insula cortex, left angular and fusiform gyrus, right middle occipital gyrus and left putamen. Using a ROI approach, I also observed greater activation under placebo compared to propranolol to black vs. white faces in right amygdala (Table 5.2 and Figures 5.3, 5.4). There were no regions that showed greater activation to black vs. white faces in the propranolol treated group as compared to placebo. In addition, for all subjects there was not greater activation when comparing white versus black faces. Decomposing the interaction (i.e., the sole comparison of black or white faces with the baseline) revealed that the activity was reduced to black faces with propranolol specifically in the dorsolateral prefrontal cortex, angular and fusiform gyrus, and simultaneously increased to white faces, specifically in the anterior insula, and in the cluster involving the amygdala.

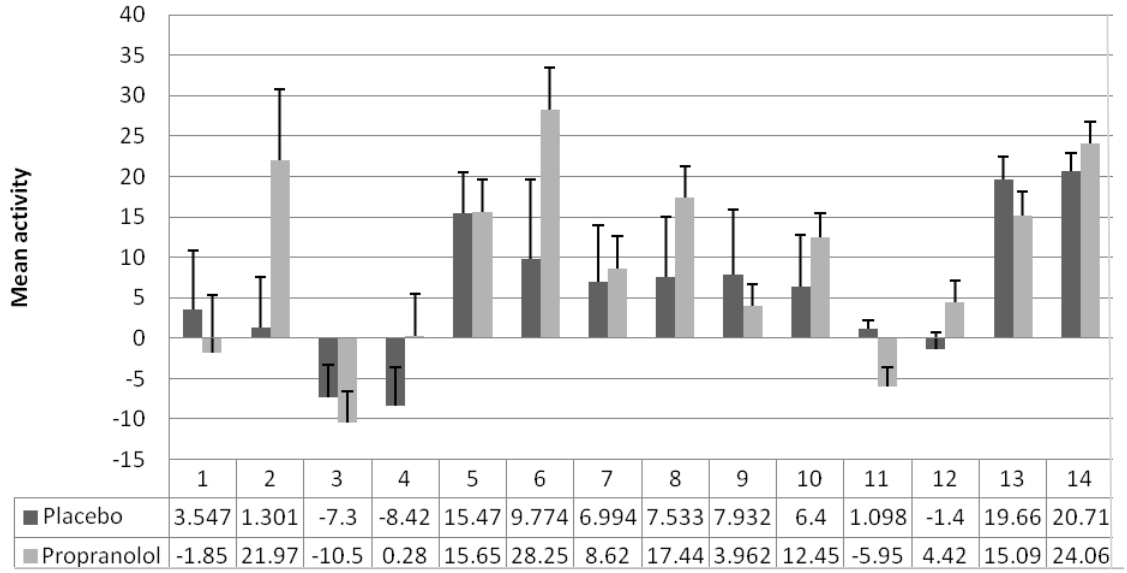
Brain region	**Cluster size (voxels)**	**Z-score**	**P-value**	***x***	***y***	***z***
Dorsolateral Prefrontal Cortex	1315	4.1	1.55E-05	10	-70	-6
Angular gyrus	852	3.85	0.000598	-60	-52	-16
Anterior insula	733	3.63	0.00169	-10	-30	0
Sub lobal regions	482	3.59	0.0185	-26	8	2
Cingulate Cortex	450	3.66	0.0258	-36	16	-20
Fusiform gyrus	444	3.56	0.0274	-34	-68	20
Middle occipital gyrus	425	3.48	0.0335	12	24	36

Table 5.2 Regions of increased activation under placebo vs propranolol for the orthogonal contrast black vs. white faces. [a] Coordinates refer to the position (x, y and z mm) for the peak voxel in each cluster according to the MNI template.

Figure 5.3 & 5.4a & 5.4b Whole brain image under placebo vs propranolol to black *vs.* white faces.




Cluster1
Cluster2
Cluster3
Cluster4
Cluster5
Cluster6
Cluster7
Mean Activation Black > White
10
0
-10
-20
-30
-40
Placebo
Propranolol
GROUP
Error bars: +/- 1 SE



	1	2	3	4	5	6	7	8	9	10	11	12	13	14
Placebo	3.547	1.301	-7.3	-8.42	15.47	9.774	6.994	7.533	7.932	6.4	1.098	-1.4	19.66	20.71
Propranolol	-1.85	21.97	-10.5	0.28	15.65	28.25	8.62	17.44	3.962	12.45	-5.95	4.42	15.09	24.06

1: Black > Baseline, Cluster 1; **2:** White > Baseline, Cluster 1; **3:** Black > Baseline, Cluster 2; **4:** White > Baseline, Cluster 2; **5:** Black > Baseline, Cluster 3; **6:** White > Baseline, Cluster 3; **7:** Black > Baseline, Cluster 4; **8:** White > Baseline, Cluster 4; **9:** Black > Baseline, Cluster 5, **10:** White > Baseline, Cluster 5; **11:** Black > Baseline, Cluster 6; **12:** White > Baseline, Cluster 6; **13:** Black > Baseline, Cluster 7; **14:** White > Baseline, Cluster 7

Figure 5.3 & 5.4a & 5.4b Whole brain image depicting greater activation under placebo vs. propranolol to black *vs.* white faces, and for the contrast with baseline Image thresholded at $Z = 2.5$, $P > 0.05$, corrected. Images are in radiological format (right brain on left).

Importantly, as Figure 5.5 shows, whole brain analysis revealed that propranolol led to reduced activity for black versus white faces in a cluster that included the amygdala. This was confirmed by using the amygdala as ROI (see Figure 5.5).

Figure 5.5 Amygdala activity under placebo for the contrast black vs. white faces.

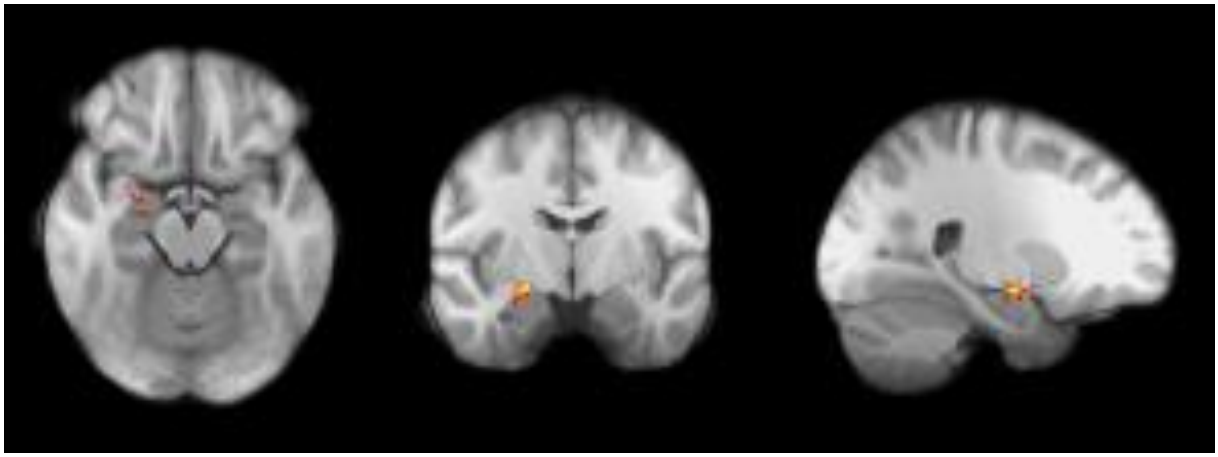


Figure 5.5 Selected sections depicting significantly greater activation in right amygdala under placebo for the contrast black vs. white faces. Images thresholded at Z = 2.3, *P*< 0.05, corrected.

For the whole sample (but not for each group separately) I found a significant positive correlation of amygdala activity (black > white) with IAT score (r = .43, p = .03). There were no significant correlations with IAT for any other brain region. Given the potential impact of propranolol on cerebral hemodynamics, it is important to differentate between regional drug effects on neural activity or global drug effects on the BOLD signal per se. To exclude the latter, I analyzed the BOLD signal change (activity versus baseline) in the primary visual cortex (V1), as elicited with a colored checkerboard. The analysis demonstrated that propranolol did not affect the signal of the V1 response.

Discussion

I found that propranolol reduced neural activation to black versus white faces in a number of brain regions involved in the processing of emotional facial expressions including the amygdala, right dorsolateral prefrontal, left cingulate and insula cortex, left angular and fusiform gyrus, right middle occipital gyrus and left putamen. Propranolol lowered IAT scores but not significantly. In addition, IAT scores were significantly correlated with activity in the amygdala for the whole sample, though not with any other region. These results extend previous work implicating the amygdala as part of a network of regions subserving outgroup perception, and support the proposal that it is a key node in the generation of implicit behavioural bias.

Phelps et al. (2000) previously found increased amygdala activity when white subjects viewed unfamiliar black faces. In addition the IAT score was positively correlated with the extent of amygdala activation so that the greater the implicit bias, the greater the amygdala activation. I have previously found that acute propranolol reduced implicit racial prejudice (see Chapter 3, and Terbeck et al., 2012), and the current study further suggests

that the same regime of propranolol lowers activity in several brain regions linked to the processing of emotional information when the implicit viewing of unfamiliar black faces is contrasted with unfamiliar white faces.

In the present study propranolol did not significantly lower IAT scores, although a clear trend was apparent (*p* one tailed = .056). Why propranolol failed to produce a significant decrease in IAT is not clear, although two possible explanations immediately suggest themselves. First, it is possible that the preceding imaging investigation, in which subjects were shown a series of black and white faces, may have altered subsequent performance on the IAT, which was carried out outside the scanner, after the imaging had been completed. In the previous behavioural propranolol study subjects viewed 120 black/white faces during the IAT task. In the current study, however, they additionally previously viewed 80 different black/ white faces in the scanner task (i.e., an increase of 67 %). Second, the sample size of the present study was smaller than in our previous study. I have calculated the effect size from the previous study (see Chapter 3, and Terbeck et al., 2012) with d = .78, which would indeed have required a larger sample to determine a significant effect *Power* = .8, p = .05, d = .78 from my previous study would require 20 subjects in each group; *Power* = .8, p = .05, d = .68 from the current study would require 28 subjects in each group). Such a large sample size is, however, difficult for fMRI research on grounds of cost and availability of subjects, especially as part of a doctoral thesis.

The brain regions in which propranolol lowered neural responses to black versus white faces have also been implicated in other fMRI studies of out-group faces. For example, Cunningham et al. (2004) found a reduction in amygdala activity and an increase in dorsolateral prefrontal cortex activity for black > white unfamiliar faces; the latter activation was greater the longer the out-group faces were presented, perhaps suggesting

an effect of cortical regulatory regions to correct for the initial implicit bias (Stanley et al., 2008). My results could be consistent with this possibility, because I found that propranolol led to deactivation not only in the amygdala but also in the dorsolateral prefrontal cortex, perhaps suggesting that lowered activation in the amygdala led to reduced need for higher order cognitive control in the prefrontal cortex.

Another brain area that might be associated with automatic activation to out-group stimuli is the insula. Here again I found that propranolol led to reduced activity for black versus white faces. Activity in the insula has not been reported in all studies using outgroup facial stimuli. However, Harris and Fiske (2006) found insula activation when subjects viewed members of extreme outgroups, such as homeless or drug addicted people, which the authors suggested might be part of an automatic disgust response. The fusiform gyrus has been strongly linked to facial processing and it has been demonstrated that this area might be relevant for the initial face processing bias for faces of different races Golby et al., 2001). The fact that propranolol lowered differential activation in this region for black versus white faces can be taken as supporting this proposal.

Although propranolol lowered neural responses to black versus white faces in several brain regions, the amygdala was the only region where activation correlated with IAT scores. This finding suggests that the amygdala may be a key brain region for generating implicit racial bias, and that propranolol may reduce implicit prejudice by suppressing amygdala activation (Terbeck et al., 2012). I did not, however, find significant correlations between IAT score and amygdala activation in either the placebo or propranolol groups considered alone but this may be due to insufficient power (see above). This finding might appear inconsistent with the investigation by Phelps et al., (2003), who reported an intact IAT effect in a single patient with amygdala lesion. One explanation for this difference between studies, however, might be that compensatory mechanisms might

have been recruited for the IAT task, in the presence of this particular brain damage. Based on previous research (Phelps et al., 2000; Terbeck et al., 2012), the current results would strongly suggest that the amygdala is a key structure for generating the implicit racial bias.

However, since the precise mechanism (e.g., a reduction in negative, or increase in positive activation patter) could not clearly be determined, and since the IAT also does not allow for the distinction between solely "Black/Bad" or "White/Good", further research is needed, for instance using neutral face comparisons in fMRI. It should be noted that previous research using black/white faces did not determine main race effects (e.g., Phelps et al., 2000), but sole correlation with the IAT behavioural measure. Additionally other fMRI research on racial basic used more elaborate design comparison (i.e., using an event related design) (e.g., Cunnigham et al., 2004, 2008), so that a race-picture and baseline comparison has not been reported previously. Thus the clear in-group out-group fMRI effect has been found to be difficult to determine, and future research is needed. Additionally, a behavioural GO-NOGO racial association test, would further allow more detailed distinctions (See Chapter 7).

In summary, I found reduced activation for several brain areas involved in the processing of emotional faces in propranolol-treated subjects who viewed black versus white unfamiliar faces. In addition, for the whole sample IAT scores, a validated measure of implicit prejudice correlated with activation to this contrast only in the amygdala. These results support the proposal that implicit aspects of racial attitudes have a causal emotional component in which the amygdala plays an important role. I suggest that noradrenergic transmission in the amygdala might be causally involved in automatic fear responses to outgroup stimuli which may then determine the extent of implicit behavioural racial bias.

CHAPTER 6: NEUROETHICS OF MORAL AND SOCIAL ENHANCEMENT

Introduction

The future possibility that pharmaceuticals might be utilised specifically to enhance normal cognitive, affective, social and moral processes has alarmed a number of people. Increasing interest and ethical debates on cognitive and emotional enhancement, might have been triggered by increased public awareness and/or and use of these technologies. For example, SSRIs are increasingly prescribed for patients whose problems might not meet the threshold for mental illness (President's Council in Bioethics). In terms of mood enhancement, Elliot (1999) stated that healthy people who took antidepressants reported that they felt energized, more alert, and more able to cope with the world. Also, Kramer (1993) suggested that individuals, who had no recognised mental illness, recovering from depression, asked to remain on treatment since antidepressants made them feel "better then well".

Pharmaceuticals may be used to enhance human beings in ways that are unacceptable because they conflict with the appropriate attitude we ought to take towards human nature, because they raise significant social justice concerns, because they may have serious side-effects, and for other reasons (Fukuyama, 2002; Kass, 2003; Sandel, 2007). Specifically, pharmaceuticals that might *morally* enhance aspects of human psychology or behaviour—for example, by producing morally better social attitudes, decisions or behaviour—have come in for especially strident criticism (Harris, 2011, 2012; Harris & Chan 2010; Sparrow, forthcoming). Most importantly, however, there are a number of pharmaceuticals already being used on a large scale which affect human cognition and emotion. In this thesis I have analysed how propranolol and reboxetine might alter individuals' psychology, and especially their *moral psychology*. However,

previously surprising little effort has been expended on research into moral effects of commonly used pharmaceuticals.

Most of the pharmaceutical effects identified for moral and social enhancement to date are relatively small, but they may nevertheless be large enough that there will be real-world situations in which they cause agents to make decisions or engage in behaviour that they would not otherwise have made or engaged in. Moreover, collectively the influence of small changes over large numbers of people may be very substantial. The demonstration that these pharmaceuticals influence important elements of moral decision-making and behaviour might motivate others to engage in the scientific and normative work of further exploring these effects, investigating other drugs for similar effects, and examining the ethics of using drugs that have these effects. Given that literally millions of doses of cognition- and affect-altering drugs are consumed annually, empirical and philosophical analysis of their moral effects is an important task.

Pharmaceuticals in current use

It must be stressed that the pharmaceuticals that this section will focus on are not the only drugs currently being used that may have effects on moral decision-making. Other pharmaceuticals, and especially those that have been investigated as general cognitive enhancers, might also have been included. Examples of such enhancers include modafinil, atomoxetine and methylphenidate. The last two, both indicated for attention deficit hyperactivity disorder (ADHD), are extremely widely prescribed: the US Drug Enforcement Administration reports around 15 million prescriptions for methylphenidate annually (DEA, 2011). Improving impulse control in ADHD has significant effects on moral behaviour, amongst other things, reducing risk of harm to others. Pramipexole, and some other dopamine agonists used to treat parkinsonism, are further examples of drugs

with morally important behavioural effects. These drugs are well known to produce pathological gambling and hypersexuality in some people, as well as, more rarely, to induce extreme paraphilias (Bostwick et al., 2009; Wolters et al., 2008). In one case, a man using pramipexole was acquitted in a case involving downloading of child porn because the court felt that this behaviour was uncharacteristic and had been induced by the drug (Irvine, 2008).

It has also not gone unnoticed that drugs employed in psychiatry in order to reduce the risks of harm have an important moral dimension. For example, Spence notes that "the antipsychotics and mood stabilisers taken by those with major psychoses, the anticraving, substitute and deterrent medications taken by those with addictions (especially disulfiram, given the serious consequences of any subsequent relapse), the antipsychotics accepted by those with personality disorders to reduce their impulsivity and aggression, the antilibidinal medicines accepted by sex offenders" may "enhance morality" (Spence, 2008, p.1). Finally, other commonly used anxiolytics—drugs used to treat disorders involving excessive anxiety—may also have morally significant effects. Specifically, since I found that propranolol reduced negative racial associations, most likely via reducing fear responses, it might be speculated that other drugs – and also alcohol – that reduce anxiety would also change social and moral judgments.

Although none of the pharmaceuticals on which I will focus were designed primarily to influence moral decision-making and behaviour, some were designed to alter other psychological states. Before proceeding to other pharmaceuticals, this Chapter will start by exploring other "moral effects" of the drug that was the first focal point of this thesis: Propranolol.

Propranolol

Propranolol has recently been investigated as a treatment or prophylactic for post-traumatic stress disorder (PTSD). The experience of traumatic events causes the release of endogenous adrenaline, which plays a role in memory consolidation (Pitnam & Delahanty 2005). Administration of propranolol, either in the immediate aftermath of a traumatic event, or at times of possible memory consolidation, might help to alleviate the symptoms of PTSD by preventing overconsolidation of memory. Building on this hypothesis, Pitman and colleagues (Pitman et al., 2002; Pitman & Delahanty, 2005) have produced evidence suggesting that PTSD may be preventable by beta-blocker administration.

Bioethicists and others have worried that the use of propranolol to treat PTSD may threaten goods we have reason to value. For instance, Hurley (2007) worries that erasing trauma blocks our epistemic access to the meaning of traumatic events, while Evers (2007) suggests that propranolol might promote what she calls mendacity: even if users recall what happened, because they have been inoculated against the emotional effects of trauma they will live as though the traumatizing events had not occurred. Recall of information is not moral judgment; rather, it is upstream of moral judgment. That is, it is an input that feeds into moral judgment. However, it is not therefore any less significant; moral decision-making processes can only work on the information which is fed into them. Evidence that Propranolol also directly influences moral and social judgments is reported in this thesis.

Selective Serotonin Reuptake Inhibitors

Whereas propranolol is typically prescribed for the treatment of somatic medical conditions, selective serotonin reuptake inhibitors (SSRIs) are prescribed for the treatment of depression and a wide range of anxiety disorders. SSRIs block the re-uptake of

serotonin in the presynaptic nerve terminal thereby increasing its activity at the synapse. Some SSRIs also have similar effects on other neurotransmitters, including noradrenaline and dopamine (Bymaster et al., 2002). They are used to alleviate depressed mood and excessive anxiety, but have also been shown to have effects on moral behaviour. For example, in rare cases, they appear to have extreme morally *negative* effects on behaviour. It has been claimed, for example, that the SSRI paroxetine has played a role in triggering violent acts such as murder in some users.[5]

Other findings show that at least some SSRIs can produce more subtle changes in social behaviour in healthy volunteers. For example, some SSRIs seem to make subjects more cooperative and less critical of others (Knutson et al., 1998). They also appear to increase social affiliative behaviour (Tse & Bond, 2002; 2003). Further experiments suggest that SSRIs also influence other fairness-related behaviour (Oosterbeek et al., 2004). As previously discussed (see Chapter 1) more recent work has been taken to suggest that potentiating serotonin increases aversion to directly causing harm to others, and thus increases deontological – or rule governed - judgments in theoretical moral dilemmas (Crockett et al., 2010).

Harm aversion is often morally praiseworthy and can lead to better moral decisions and behaviour—indeed, both psychopaths and normal individuals who have psychopathic tendencies tend to be less averse to harming other individuals in the 'personal' moral scenarios described above (Bartels & Pizarro, in press; Koenigs et al., in press). It is to be expected that a reduced aversion to harming others will often have highly antisocial effects. In some circumstances, however, it may nevertheless be desirable for people to be willing to inflict harm on others (or at least accepting of the need to do so). Punishment for

[5] http://www.healyprozac.com/academicstalking/Post%2019%20-%20Cowen%20Review%20of%20Panorama%20Secrets%20of%20Seroxat.htm

the violation of social and legal norms involves the infliction of harm on unwilling victims; such punishment is arguably needed for the maintenance of fair institutions and social trust. Whether SSRIs cause morally better or morally worse behaviour depends on many factors, including the pre-existing dispositions of subjects who take them, and the range of cooperative or conflictual interactions into which they are likely to enter. For example, we would not want judges and jurors to be extremely averse to imposing harm, but we might value different dispositions in social workers and doctors. It is not yet clear whether the effects of SSRIs on moral decision-making and behaviour are on the whole positive or negative. This is a matter for further research and debate.

Oxytocin

The hormone and neurotransmitter oxytocin is best known for its somatic effects—it facilitates birth and breastfeeding in humans and other mammals—but it also influences morally-significant behaviour. It is released by the oral contraceptive pill and glucocorticoids used for the treatment of asthma. For example, in non-human mammals oxytocin appears to mediate pair bonding, maternal care, and other pro-social behaviour (Insel & Fernald, 2004), and recent studies suggest that it plays a role in mediating trust, co-operation, empathy and generosity in humans. For example, investors administered oxytocin exhibited significantly more trusting behaviour—that is, they entrusted the trustee with a significantly greater amount of money (Kosfeld et al., 2005).

The ethical picture is further complicated by the fact that oxytocins effects on trusting and other 'pro-social' behaviour towards others appear to be sensitive to the group membership of those others. Experiments by De Dreu's group indicate that oxytocin can also *reduce* pro-social behaviour towards out-group members where this helps one's in-group. Administration of oxytocin to subjects prior to their participating in a group-based

financial game induced 'tend and defend' reactions: it increased trust and co-operation within groups, but also increased non-co-operation with (though not aggression against) members of other groups when this helped to protect one's in-group (De Dreu et al., 2010).

This work suggests that the so-called 'pro-social' effects of oxytocin might be more aptly characterised as 'pro-in-group' effects since the hormone can in fact induce anti-social behaviour when this conduces to the interests of one's in-group. Increased bonding within a family might be beneficial, and might help with the moral development of children. But in-group favouritism, while seemingly benign, may also drive many of contemporary society's greatest evils, such as genocide and terrorism, as well as more mundane but pervasive problems like class and race differences in wealth, health and political power. Given this fact, and assuming that the effects of oxytocin are replicable and robust, it seems doubtful whether drugs that increase oxytocin levels would have ethically desirable effects on behaviour even if they motivate more pro-social behaviour within groups. Again, however, this is likely to be context dependent. For example, in circumstances where an individual regards humanity as a whole as her in-group, the effects of elevated oxytocin levels may be less problematic than where 'in-group' is understood in narrower ways. It should be stressed that how agents draw the lines between in-group and out-group appears to be sensitive to context (Gaertner, 2000; Turner et al., 1987). Table 6.1 gives an overview of further widely used pharmaceuticals with possible moral side effects.

Drug (class)	Main Current Use(s)	Possible Morally Significant Effects
Alcohol	Recreational	Impulsivity Hostility Reduced social inhibition Impaired ability to drive
Amphetamines	Recreational Enhancement of attention and alertness Treatment of ADHD Narcolepsy	Increased or reduced activity Increased or reduced restlessness Reduced distractability Excitation Hostility and aggression Paranoid behaviour Drug-seeking behaviour due to addiction
Anti-psychotics	Treatment of psychotic disorders such as schizophrenia	Prevention of paranoid, disorganized behaviour and lack of motivation associated with psychosis Restlessness
Atomoxetine (SNRI)	Treatment of ADHD	Reduced classroom rule violation Reduced impulsivity Obsessive behaviour Psychosis and mania and associated behaviours
Benzodiazepines	Treatment of Anxiety disorders Insomnia Seizures Recreational	Reduced anxiety Aggression Impulsivity Reduced motivation (chronic use) Reduced attention Drug-seeking behaviour due to addiction
Cannabinoids	Recreational Treatment of	Reduced attention Reduced inhibitions

	Nausea from chemotherapy AIDS related anorexia	Impaired driving ability Impaired short-term and working memory Impaired learning Panic reactions, paranoia and psychosis Illusions of increased insight
Citalopram (SSRI)	Treatment of Major depression Anxiety disorders	Increased motivation due to treatment of depression Reduced anxiety Triggering violence Increased co-operation Reduced criticism of others Fairer distribution of resources Reduced rejection of unfair offers Increased aversion to harming others (in highly empathetic individuals)
Cocaine	Recreational Local anaesthesia	Drug-seeking behaviour due to addiction Increased friendliness Increased activity Disruption of fear conditioning Increased confidence Irritability, anxiety, agitation and suspicion (in withdrawal)
Combined Oral Contraceptive Pill	Contraception Treatment for Polycystic ovary syndrome Endometriosis Painful menstruation Acne	Reduced motivation due to depression May increase oxytocin secretion, which may cause Increased trust Increased trustworthiness Increased co-operation within in-group Reduced co-operation with out-groups

Disulfiram	Treatment for alcohol abuse	Reduced alcohol use
Glucocorticoids	Treatment for Asthma Autoimmune conditions	Improved concentration and vigilance Memory impairment Improved memory for emotionally arousing events May increase oxytocin secretion, which may cause: Increased trust Increased co-operation within in-group Reduced co-operation with out-groups
L-dopa	Treatment of Parkinson	Excitement Confusion Psychosis Agitation and anxiety
Lithium	Treatment of Bipolar disorder	Reduced paranoia, grandiosity and risk-taking due to treatment of mania Increased motivation due to prevention of depression
Methylphenidate	Treatment of ADHD Narcolepsy	Increased attention Improved working memory Psychosis Confusion Irritability Effects on dopamine-based reward system
Modafinil	Cognitive enhancement Treatment of Narcolepsy Shift work sleep disorder Excessive daytime	Increased alertness and attention Improved working memory Anxiety Aggression

	sleepiness	Effects on dopamine-based reward system
Opiates	Pain relief Anaesthesia Treatment of Cough Diarrhoea Irritable bowel syndrome Opiate addiction Recreational	Confusion and mental clouding Restlessness Excitement Drug-seeking behaviour due to addiction
Pramipexole	Treatment of parkinsonism	Pathological gambling Hypersexuality Paraphilias (e.g. paedophilia) Compulsive behaviours (e.g. compulsive shopping and cross-dressing)
Propranolol (β-blocker)	Treatment of: Hypertension Angina Migraine Arrhythmias Myocardial infarction Reduction of anxiety	Reduced memory consolidation Reduced emotional effect of psychological trauma Conservative bias (reduced risk-taking) in memory tasks Effects on fear and disgust reactions and thus on moral judgment and implicit bias against outgroup members

Table 6.1 Possible Moral Effects of Some Widely Used Pharmaceuticals

Discussion

The evidence reviewed above is a small slice of the data available on the ways in which pharmaceuticals modulate moral decision-making, as well as the upstream influences on such decision-making and its downstream implementation. In some cases, the effects on cognition and behaviour appear to be rather small. However, where drugs are widely used, even small moral effects on individuals should not be ignored, since they might aggregate to have a serious impact. Many of the most serious challenges currently facing humanity—climate change, pollution, global poverty, and war—can all, arguably, be attributed to widespread but relatively minor moral failings (Savulescu & Persson, 2012). Small changes in the degree to which large segments of the population are concerned about the long term future, are inclined towards out-group aggression, or are altruistic towards spatially and temporally distant strangers might massively aggravate or mitigate these problems. Similarly, small differences in trust or out-group aversion could have large effects on the results of elections where candidates differ in their ethnic group or perceived trustworthiness. The possibility of such aggregation makes the scientific and ethical assessment of the moral effects of widely used drugs, such as contraceptives, painkillers, anti-depressants and medications used to lower blood pressure, a matter of great practical importance. There is a need to determine what the moral effects of these drugs are, and whether they are ethically desirable.

Existing evidence suggests an ethically mixed picture: in some ways, pharmaceuticals might produce morally better decisions and behaviour—for instance, by increasing pro-sociality—and in other ways the very same pharmaceuticals might cause a moral decrement in decisions and behaviour. Whether using a particular pharmaceutical induces morally better or worse decisions and behaviour depends, crucially, on the individual's pre-existing dispositions and the circumstances in which they act, as well as

what the drug is used for and the effect of any underlying condition on moral decision-making and behaviour. For example, the costs and benefits of propranolol are context-dependent. We need to compare the cognitive capacities and dispositions of the agent prior to propranolol use to those she exhibits under its influence, and also to consider the range of circumstances in which she is likely to be required to make moral decisions. Whether propranolol use is advisable or obligatory, permissible or impermissible, will depend on a range of factors, some of them extremely hard to assess.[6] Similar thoughts apply to drugs that elevate levels of oxytocin. Whether use of such drugs is desirable, from a moral point of view, may depend on factors such as how trusting or co-operative an individual is to begin with, how trustworthy others are, how sharply in-group/out-group distinctions are drawn, and how effects on individuals might aggregate if these drugs are widely used.

It should also be stated that the scientific evidence for the effectiveness of pharmacological mood enhancement is still controversial. In an extensive meta-analysis Repantis et al. (2009) reviewed 65 studies using antidepressant drugs in healthy volunteers, and concluded that there was no consistent evidence for enhancing effects on mood, emotional processing, wakefulness, attention, memory, or executive functions. Additionally, a recent meta- analysis found that antidepressant treatment was only more effective than placebo in severe but not mild or moderate depression (Kirsch et al., 2008). The main argument against using psychotropic medication solely for enhancing proposes concerns the side effects (Sahakian & Morein-Zamir, 2007) which would have to be weighed against the benefits in every case individually. But, as Farah and Wolpe (2004) suggest, perhaps one should value life in its imperfections.

[6] Even if a reduction in implicit negative bias against outgroups is thought to be an unqualifiedly positive effect, the reduction in fear that accompanies it might, in many contexts, lead to rather more negative consequences.

It is thus a far more pressing concern that we investigate the effects of pharmaceuticals currently being used on a large scale. These pharmaceuticals may already be influencing the shape of our societies, for better or for worse. We need urgently to discover how they influence moral decision-making and behaviour, so that we avoid the worst dangers they pose for us, and perhaps harness them to better ends. Investigation cannot be limited to psychopharmaceuticals, since a range of pharmaceuticals prescribed for somatic conditions may also have effects on the brain and mind. Many chemicals involved in the regulation of somatic processes are also involved in the regulation of neural processes: serotonin, for instance, is involved in cardiovascular regulation, respiration, sleep-wake cycles as well as appetite, pain sensitivity, and reward learning (Churchland, 2011). The research findings reported in this thesis in relation to propranolol have important social and ethical implications. And propranolol is just one example of a commonly used drug which can affect moral choices and social outcome

CHAPTER 7: GENERAL DISCUSSION

Introduction

In this interdisciplinary thesis the role of noradrenaline in moral and social judgments was investigated. It was determined that beta adrenergic blockade, via propranolol, led to an increase in deontological moral judgments (see Chapter 2). Moral judgments were also formed more quickly and subjects were more decisive. These findings suggest that primary emotional arousal might be involved in processes of harm aversion. The results are in contrast to theories suggesting that deontological moral judgments are more emotionally engaging than utilitarian decisions. I have argued that the involvement of emotion in moral judgments might be more complex than previously suggested. Specifically, primary and secondary emotions might play a different role in the moral decision making process. Further, the role of noradrenergic enhancement, via reboxetine, on moral judgments was investigated (see Chapter 4). Based on the previous result using propranolol, it was predicted that reboxetine intervention might lead to an increase in utilitarian judgments. However, the study did not demonstrate such an effect. I have argued that the effect of reboxetine might, even though it is pharmacologically complementary to propranolol, not necessarily lead to complementary behavioural changes. The possibility was discussed that reboxetine might have led to an increase in positive emotional arousal and not to an increase in negative emotional arousal, such as fear responses. This would suggest that specifically a reduction in primary *negative* emotional arousal, as associated with propranolol intervention, would lead to changes in theoretical moral decisions. I will end this thesis with a discussion of whether the use of theoretical moral dilemmas to assess individuals' moral judgments is the state-of-the art research method in moral psychology. Future research will be suggested that might utilise more realistic moral judgment tasks or investigate moral behaviour, rather than moral decision making. It will be suggested that

moral behaviour might be investigated using paradigms from social psychology that assess pro-social behaviour.

The role of noradrenaline in social judgments, and specifically in racial attitudes, was also investigated (see Chapters 3 and 5). Most importantly, I found that beta adrenergic blockade led to reduced implicit but not explicit racial associations. However, noradrenergic enhancement with reboxetine did not lead to an increase in negative implicit racial associations (see Chapter 4). Again, I have argued that even though reboxetine showed the physiological effect of increased heart rate, it might not have increased negative emotional arousal but, rather, enhanced positive emotional processing. Next, the results of a pharmacological fMRI were reported (see Chapter 5). The study further explored the underlying neural mechanisms of reduced negative implicit associations with beta adrenergic blockade. I found that propranolol led to reduced activity in amygdala, insula, fusiform gyrus, and the dorsolateral prefrontal cortex for black compared to white facial stimuli, specifically, when comparing black or white facial stimuli to baseline, it was determined that propranolol reduced activity to black and increased activity to white faces within different regions. Importantly, only the amygdala activity was correlated with the implicit racial bias. It was proposed that this research delivers the first evidence that primary emotional arousal, such as fear responses, might play a *causal* role in implicit racial associations, with the amygdala generating the implicit bias. In the following I will suggest future social psychological research based on these findings.

Involvement of noradrenaline in moral and social judgments

The research suggests that noradrenergic mediated arousal might be involved in higher order social and moral processes. Numerous previous research has already demonstrated that noradrenaline is strongly related to automatic emotional arousal, and

basic affective states, specifically fear responses (e.g., Bliss et al., 1968; Corrodi et al., 1968; Hurlemann et al., 2010; van Stegeren et al., 2005). For example, in Chapter 1 reviewed how noradrenaline mediates fight and flight responses.

Some previous research and theories have also suggested that basic emotions might be involved in moral and social judgments. For example, Phelps et al. (2000) found subjects' IAT scores predicted amygdala activity towards black unfamiliar faces. Regarding morality, Greene et al. (2001) demonstrated that activity in emotion processing brain areas of the brain was associated with deontological moral decisions. Using the novel approach of pharmacological fMRI (i.e., to study the effects of drug intervention with neuroimaging) further evidence for the *causal* role of emotional arousal in higher order processes was determined in this thesis. Thus, the thesis suggests that noradrenergic mediated primary emotional arousal, and possibly specifically negative emotional activation, increases harm aversion and reduces negative racial associations. It was thus demonstrated that besides secondary emotions, such as guilt and shame, also basic primary emotions, such as fear, can have an effect on higher order psychological processes.

Limitations of the research

One limitation of the research might be that all studies used a between-groups design. On the one hand using a within-group design increases statistical power, however, on the other hand, the reliability of the results might be reduced since subjects have to complete the same task twice and since carry-over effects might be expected (i.e., the effects from the previous treatments may still be present when delivering new treatment, thus affecting the outcome of the new treatment). For example, it has been demonstrated that subjects sometimes perform differently on the IAT when completing it for a second time, especially because they might become aware of the nature of the task (i.e., they might

become suspicious that "prejudice" is being tested) (e.g., Nosek et al., 2007). Indeed, it has been shown that even though the IAT is suggested to be an unobtrusive measure of racial bias, knowledge of what is being tested can influence the results (see Nosek et al., 2007 for a review). Additionally, regarding the moral judgments task, it is likely that subjects would try to be consistent in moral choices, and thus give the same answer if confronted with the same moral dilemma a second time. Therefore, a within group design seemed impractical and unreliable for this research.

A second limitation might arise regarding the moral dilemma task. Even though theoretical moral dilemmas are currently still the most prominent method to investigate moral decision-making, the use of theoretical moral dilemmas to research moral judgments might have significant problems. Numerous researchers have criticised the use of theoretical moral dilemmas for research in moral psychology (e.g., Hueber et al., 2008; Joyce, 2008; Nichols, 2005). For example, critics have stated that the moral dilemmas are too artificial (how often do people happen to be confronted with an out of control trolley on the train tracks, and a fat man on the bridge next to them) (e.g., Hueber et al., 2008; Joyce, 2008; Nichols, 2005). The criticism might however not be significant if researcher carefully limit the interpretations of the moral dilemma task. The moral dilemmas are designed to assess what individuals theoretically regard as morally acceptable (i.e., the dilemmas are designed to determine how individual`s arrive at decisions about what one ought to do/ what is ethically right), and thus the answers do not indicate what people *would actually do* when encountering the situation in real life. However, some studies sometimes seem to confuse the two dimensions. For example, some studies use different moral dilemma questions. While some researchers ask the subjects, "Is it morally acceptable?" others ask, "Would you do it?" (Moll et al., 2002; Young & Koenigs, 2007). Indeed, I found an effect of propranolol on moral judgments as only when subjects were

asked about theoretical moral acceptability, but not when they were asked about performance (i.e., the question whether subjects would themselves perform this action) (see Chapter 2). That moral decision might not equal moral action is also demonstrated, for example, by Milgram (1963). Migram found that even though all subjects announced that, in principle or in the abstract, they would not obey an order and give highly painful shocks to another individual, when faced with just that situation in a highly-involving, 'high impact' experimental task, the majority of individuals did just that.

Another method of studying moral decision making is to use real life moral dilemmas (i.e., those that subjects report to have experienced themselves) (e.g., Krebs, Denton, & Walk, 1997). Researchers have argued that real life moral dilemmas have more relevance, and are therefore more engaging than hypothetical moral conflicts (e.g., Krebs et al., 1997). A first attempt to produce a standard set of real life moral scenarios has been made by Knutson et al. (2010). Knutson et al. developed standard moral vignettes that are all based on real life events (e.g., Is abortion morally acceptable?). The standard dilemmas vary on a number of dimensions including emotional intensity, degree of social norm violation, and level of harm/benefit caused. However, besides the effort, the traditional hypothetical moral dilemmas (e.g., trolley dilemma) are still mostly used by current researchers. In order to make the results of my research comparable to other relevant studies (e.g., Greene et al., 2001) I thus decided to also use the same conventional theoretical moral dilemmas. Generally however, it might be suggested that research in moral psychology per se might advance further if methods and the operationalization of morality would be improved.

The paper published based on my research on propranolol and implicit racial bias (see Chapter 3) was followed by a commentary, suggesting that the IAT might not be a reliable measure to assess racial "prejudice" (Burchett & Glenn, 2012). Indeed, the IAT

was suggested to measure racial *associations* and it is difficult to infer if this might be equivalent to using the term implicit *prejudice*. However, there is a considerable amount of research supporting the reliability and validity of the IAT (see Greenwald et al., 2003 or Nosek et al., 2007, for reviews). Additionally, Cunningham, Preacher, and Banaji, (2001) reported consistency, and convergent validity specifically for the racial IAT measure. Further, IAT scores have been shown to predict subtle but significant differences in behaviour towards out-group members, such as the frequency of positive versus negative words being used in a conversation (Nosek et al., 2007). Further research is, however, needed to determine if changes in implicit associations with propranolol also lead to behavioural changes towards out-group members. Racial attitudes are complex, consisting of explicit/cognitive and implicit/emotional as well as behavioural aspects. Propranolol was found to have an effect on the implicit aspect of racial attitudes but it would still need to be determined if this might also lead to follow-up changes in behaviour, as well as ultimate changes in explicit attitudes. Indeed it might be speculated that, in accordance with cognitive dissonance theory (Brehm & Cohen, 1962) (i.e., competing reactions, such as not liking something but still doing it, can lead to tension, which might be resolved by attitude changes) initial changes in implicit attitudes might indeed – over time – lead to changes in explicit attitudes as well. For example, implicit association changes might also lead to subtle behavioural changes, which then might increase the tension between those behavioural changes and the explicit attitudes, which would then be changed accordingly.

Future directions

The research on the effect of noradrenaline on moral and social judgment was the first ever investigation determining the influence of pharmacologically manipulated noradrenaline transmission on higher order social processes. This research has opened a new field of interdisciplinary investigation and numerous follow-up studies could extend

this research. In the following I will propose three lines of research that might follow the thesis.

First, the effect of propranolol on implicit attitudes might be investigated further; for example, the effect of long-term propranolol use should be studied, since it still remains unknown if continuous treatment with propranolol would have similar and persisting effects on attitudes and moral judgments. Additionally, since the effect of propranolol on racial associations was researched, it is also unclear if other "prejudices", such as religious, or gender attitudes would also be affected by propranolol intervention. Since it was determined that stigma against other minorities, such as obese, or transsexual people, also led to an increase in amygdala and insula activation (see Stanley et al., 2008, for a review) attitudes towards these target groups might have similar underlying automatic emotional aspects. For example, it has been shown that there is gross health disparity (i.e., discrimination in health care) in the UK, as well as other European countries, which is based on race/ethnicity, socioeconomic status, age, or religion (Bécares, Stafford, & Nazroo, 2009). Considering the specific case of race, studies have demonstrated that white physicians spend significantly less time for health intervention with black compared to white patients (Oliver, Goodwin, Gotler, Gregory, & Stange, 2001). In particular, Penner et al. (2010) found that physicians who scored high in implicit but low in explicit prejudice held interactions with black patients that were least satisfying for the patients compared to any other combination of explicit and implicit prejudice. It might thus be researched if this unequal treatment in an applied setting could also be intervened with propranolol.

Indeed, there is also the open question of whether a reduction in subjects' IAT score would correspond to changes in subjects' concrete behaviour towards out-group members. It has been shown that implicit associations predict subtle behaviour, such as friendliness, and unobtrusive pro-social acts (Nosek et al., 2007). Since propranolol

reduces emotional arousal, which corresponds to a reduction in implicit attitudes (Terbeck et al., 2012; see Chapter 3) propranolol should also decrease anti-social behavioural responses to out-group members.

Secondly, further research might explore the precise interaction of secondary and primary emotions in morality and racial associations. Recently, Crockett et al. (2010) found that SSRI citalopram had an effect on moral decision making (i.e., increasing harm aversion/ deontological moral judgments). They suggested that serotonin was involved in processing of social stimuli, in empathy responses, and pro-social behaviour (Crockett et al., 2010). Propranolol, on the other hand, has been shown to effect primary emotional responses, such as fear (Hurlemann et al., 2010). An fMRI study might be employed to research the involvement of specific brain areas associated with SSRI compared to propranolol intervention during moral jugdments but also during the passive viewing of out-group stimuli. Recent work has demonstrated that the amygdala activation towards out-group stimuli was reduced, mediated by an increase in prefrontal cortex activity, for example when racial faces were presented for longer durations (Cunningham et al., 2004). It might be expected that SSRI intervention would also reduce the racial bias, but via a different neural mechanism compared to propranolol (e.g., via an increase in prefrontal cortex activity).

Thirdly, and ultimately one might want to research the neural basis of pro-social behaviour (rather than theoretical moral judgments). It has been suggested that anonymous donations to charities – a costly pro-social act without obvious personal gain – delivers a good method to study "pure" altruism (e.g., Andreoni, 1990). Importantly, Moll et al. (2008) found activity in two distinct brain networks during charitable donation decisions. First, activity was found in the ventral stratium. This result was striking, since the same brain activation pattern was also found for personal monetary rewards (Moll et al., 2008).

The finding thus suggested that giving to charity can be intrinsically rewarding. Secondly, Moll et al. (2008) found activation in the medial and lateral orbitofrontal cortex, and suggested that this activity might be interpreted as being associated with processing of social stimuli, and thus that social attachment also played a role in donation decisions. McCabe, Mishor, Cowen, and Harmer, (2010) studied the effect of citalopram on reward processing and found that SSRI reduced activity in the ventral striatum during reward processing. Thus it might be suggested that citalopram would *reduce* the intrinsic value of social rewards, such as donations to charities. In their study, Crockett et al. (2010) found that citalopram increased deontological decisions and rejection rates of unfair offers in the Ultimatum game. The authors suggested that citalopram increased harm aversion. Crockett et al. (2010) also speculated that citalopram actually *increased* empathy. It is a very interesting question to determine if antidepressant treatment would "only" reduce negative affect (such as aggression) or actually enhance positive affect (such as empathy), as might also have been the case with the reboxetine intervention. Overall the aim might be to distinguish the effect of primary versus secondary emotions on processes of social and moral judgments, and to develop a new approach to studying the neural basis for social behaviour and higher order judgments and attitudes.

Concluding remarks: Means of reducing racial prejudice

The novel research finding that propranolol reduces implicit racial bias gives new insights into the role of automatic emotional arousal, such as fear responses, in implicit racial associations. One might infer from this research that indeed social-political programs that are designed to reduce racial prejudice, and that particularly focus on the aspect of reducing intergroup anxiety, might be a successful means to reduce negative racial bias. For example, extensive research has demonstrated that intergroup contact can reduce explicit and implicit prejudice, also by means of reducing intergroup anxiety (e.g.,

Hewstone et al., 2002; Pettingrew & Tropp, 2008). Research into the processes underlying racial prejudice is essential for society, and prevention and reduction of unequal treatment and discrimination of minority group are an important aim for today's multicultural global society. Also one might debate whether, if further research confirms the effect of pharmacological intervention on racial attitudes and behaviour, these medications might be considered as part of a 'therapy' prescribed for reducing extremist racial behaviour, especially if the negative attitude was associated with insulting, even violent, behaviour towards others who belong to that category. For example, recently, a woman was prosecuted for shouting racial abuse at fellow passengers on an underground train in south London (retrieved from: http://www.guardian.co.uk/technology/2011/dec/06/christmas-prison-women-tram-youtube).

If fear is involved in racial prejudice, then it will be an important step to reduce it. It should thus be one essential step to research basic emotions in reasoning and in higher order social processes since:

> *"The lower levels in the neural edifice of reason are the same ones that regulate the processing of emotions and feelings, along with the body functions necessary for an organism's survival. In turn, these lower levels maintain direct and mutual relationships with virtually every bodily organ, thus placing the body directly within the chain of operations that generate the highest reaches of reasoning, decision making, and, by extension, social behaviour and creativity. Emotion, feeling and biological regulation all play a role in human reason."* (Damasio, 1994, p. xvii).

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Appendix 2.1

Case Record Form

CASE RECORD FORM

Participant Initials: **ID number:**

Study Identifiers:

Research Ethics Committee:	Oxford NHS
Medicinal Product:	Propranolol
Funding:	University of Oxford
Investigators:	Mag. Sylvia Terbeck Professor Miles Hewstone Professor Phil Cowen & Dr Sarah McTavish Professor Julian Savulescu & Dr. Guy Kahane
Study Location:	University Department of Psychiatry, Warneford Hospital, Oxford OX3 7JX

MISSING DATA

Please record below any instance where the data has NOT been recorded for the participant.

Form	Visit	Reason

SCREENING

(VISIT 1)

PARTICIPANT NUMBER:

Visit Date:

dd/mm/yy

Participant name:

Address:

Phone Numbers (circle preferred number):

Home:

Mobile:

Work:

E mail:

APPENDIXES

How often do you check your email?

GP details for our information

GP Name:

GP Address:

DEMOGRAPHY

Date of Birth:

dd/mm/yy

Gender: Male/Female

Occupation:

Ethnicity:

Height (cm):

Weight (kg):

Body Mass Index*:

Average caffeinated drinks/day:

(coffee, tea, cola, redbull, caffeine tablets)

Average cigarettes/day:

Average units of alcohol/week:

Max units consumed on single occasion:

*Body Mass Index calculated using the following formula

$$\text{Body Mass Index} = \frac{\text{Weight (kg)}}{(\text{Height (cm)})^2} \times 10{,}000$$

SIGNIFICANT MEDICAL/SURGICAL HISTORY

Is the participant suffering from or has he/she ever suffered from any significant medical or surgical condition?

YES/NO

If yes, list below:

Diagnosis	Year of first diagnosis	Resolved	Ongoing

PRIOR MEDICATION

Has the participant taken any medication (prescribed, OTC, vitamin supplements, illicit) within the month PRIOR to screening?

YES/NO

If 'YES', please record the medications below.

Drug Name	Dose	Frequency	Route	Indication	Duration of Therapy	End Date	Continuing at end of study?

Has the participant taken any illicit drugs at any time in the past?

YES/NO

If 'YES', please record the drugs below.

Allergies

Does the participant suffer from any allergies, including lactose intolerance and nut allergies?

YES/NO

If ‘YES’, please record the details below.

Family psychiatric history

Does the participant know of any (first degree) relative who suffers from a psychiatric illness or who has seen a psychiatrist for any reason?

YES/NO

If ‘YES’, please record the details below.

Pregnancy/breastfeeding

Is the participant currently pregnant or breastfeeding?

YES/NO N/A

Menstrual cycle

Length of cycle

Regular/irregular

Date of last menstrual period

Predicted date of next period

Structured Clinical Interview for DSM-IV Axis 1 Disorders (SCID-V)

Has the SCID been completed?

YES/NO

Document any 'yes' responses below:

Beck Depression Inventory

Has the BDI been completed?

Score? ……..

Eysenck neuroticism scale

Has the Eysenck scale been completed?

Score? ……..

ECG

Has the ECG been completed?

YES / NO

Have a labelled copy been attached to the CRF?

YES / NO

For Doctor to complete:

Have sections detailing PMH, PΨH, FΨH, drug Hx, SCID been completed and positive responses checked? –

YES / NO

Is there in particular any history cardiovascular disease or of asthma?

YES / NO

Were any new symptoms described in response to direct questions?

(re: CNS, CVS, RS, GIS)

YES / NO

Please enter any details:

Has the ECG been checked and is it satisfactory?

YES / NO

Physical Examination

CVS pulse BP: sitting standing

RS

Other

Based on the above:

Is the participant medically fit for inclusion in the study?

YES / NO

Signed: …….

ELIGIBILITY CHECKLIST

Does the subject meet the following eligibility criteria?

Answer the following questions by marking the appropriate box.

Inclusion Criteria	Yes	No
1. Is the participant aged between 18-45 years inclusive?		
2. Has the participant provided written informed consent?		
3. Does the participant have a BMI between 19-30 ?		
4. Is the participant physically fit, as assessed by medical practitioner?		
5. Is the participant a fluent English speaker?		
6. Is the participant able to comply with study requirements?		
6. Has the participant not taken part in a similar study before?		

If the answer to any of the above is **NO** the subject must be excluded from the study.

ELIGIBILITY CHECKLIST

Does the subject meet the following eligibility criteria?

Answer the following questions by marking the appropriate box.

Exclusion Criteria	**Yes**	**No**	**NA**
1. Does the participant have significant active medical conditions which in the opinion of the Principal Investigator could introduce additional risk factors and/or interfere with study procedures?			
2. Are they or do they intend to become pregnant or are they breastfeeding?			
3. Does the participant have current or previous Axis 1 disorder on DSM-IV (including alcohol or drug dependency) (excluding adjustment disorder)?			
4. Is the participant taking any psychoactive medication?			
5. Is the participant taking propranolol or any other beta blocker?			
6. Has the participant taken part in any psychological or medical studies involving the use of medication within the past 3 months?			

If the answer to any of the above is **YES** the subject must be excluded from the study.

Has the subject been given the following?

Answer the following questions by marking the appropriate box.

	YES	NO
Participants Information Sheet		
Copy of the Consent Form		

Have travel arrangements been made for transport on Test Day?

YES / NO

END OF SCREENING VISIT

Appendix 2.2

Visual Analogue Scales

PN: **NUMBER:**

AT THE MOMENT I FEEL

TENSE

_____

Not at all extremely

ANGRY

_____

Not at all extremely

SAD

_____

Not at all extremely

HAPPY

_____

Not at all extremely

ALERT

_____

Not at all extremely

TIRED

_____

Not at all extremely

Appendix 2.3

Moral Judgments A

Impersonal Moral Scenarios:

1. Standard Trolley

You are at the wheel of a runaway trolley quickly approaching a fork in the tracks. On the tracks extending to the left is a group of five railway workmen. On the tracks extending to the right is a single railway workman. If you do nothing, the trolley will proceed to the left, causing the deaths of the five workmen. The only way to avoid the deaths of these workmen is to hit a switch on your dashboard that will cause the trolley to proceed to the right, causing the death of the single workman.

How morally acceptable is it to hit the switch in order to avoid the deaths of the five workmen?

Would you hit the switch in order to avoid the deaths of the five workmen?

2. Standard Fumes

You are the late-night watchman in a hospital. Due to an accident in the building next door, there are deadly fumes rising up through the hospital's ventilation system. In a certain room of the hospital are three patients. In another room there is a single patient. If you do nothing the fumes will rise up into the room containing the three patients and cause their deaths. The only way to avoid the deaths of these patients is to hit a certain switch, which will cause the fumes to bypass the room containing the three patients. As a result of doing this, the fumes will enter the room containing the single patient, causing his death.

How morally acceptable is it to hit the switch in order to avoid the deaths of the three patients?

Would you hit the switch in order to avoid the deaths of the three patients?

3. Vaccine Policy

You work for the Bureau of Health, a government agency. You are deciding whether or not your agency should encourage the use of a certain recently developed vaccine. The vast majority of people who take the vaccine develop an immunity to a certain deadly disease, but a very small number of people who take the vaccine will actually get the disease that the vaccine is designed to prevent. All the available evidence, which is very strong, suggests that the chances of getting the disease due to lack of vaccination are much higher than the chances of getting the disease by taking the vaccine.

How morally acceptable is it to direct the agency to encourage the use of this vaccine in order to promote national health?

Would you direct your agency to encourage the use of this vaccine in order to promote national health?

4. Speedboat

While on vacation on a remote island, you are fishing from a seaside dock. You observe a group of tourists board a small boat and set sail for a nearby island. Soon after their departure you hear over the radio that there is a violent storm brewing, a storm that is sure to intercept them. The only way that you can ensure their safety is to warn them by borrowing a nearby speedboat. The speedboat belongs to a miserly tycoon who would not take kindly to your borrowing his property.

How morally acceptable is it to borrow the speedboat in order to warn the tourists about the storm?

Would you borrow the speedboat in order to warn the tourists about the storm?

5. Guarded Speedboat

While on vacation on a remote island, you are fishing from a seaside dock. You observe a group of tourists board a small boat and set sail for a nearby island. Soon after their departure you hear over the radio that there is a violent storm brewing, a storm that is sure to intercept them. The only way that you can ensure their safety is to warn them by borrowing a nearby speedboat. The speedboat belongs to a miserly tycoon who has hired a fiercely loyal guard to make sure that no one uses his boat without permission. To get to the speedboat you will have to lie to the guard.

How morally acceptable is it to lie to the guard in order to borrow the speedboat and warn the tourists about the storm?

Would you lie to the guard in order to borrow the speedboat and warn the tourists about the storm?

APPENDIXES

Personal Moral Scenarios:

6. Transplant Low-conflict

You are a doctor. You have five patients, each of whom is about to die due to a failing organ of some kind. You have another patient who is healthy. The only way that you can save the lives of the first five patients is to transplant five of this young man's organs (against his will) into the bodies of the other five patients. If you do this, the young man will die, but the other five patients will live.

How morally acceptable is it to perform this transplant in order to save five of the patients?

Would you perform this transplant in order to save five of your patients?

7. Footbridge High-conflict

A runaway trolley is heading down the tracks toward five workmen who will be killed if the trolley proceeds on its present course. You are on a footbridge over the tracks, in between the approaching trolley and the five workmen. Next to you on this footbridge is a stranger who happens to be very large. The only way to save the lives of the five workmen is to push this stranger off the bridge and onto the tracks below where his large body will stop the trolley. The stranger will die if you do this, but the five workmen will be saved.

How morally acceptable is it to push the stranger on to the tracks in order to save the five workmen?

Would you push the stranger on to the tracks in order to save the five workmen?

8. Crying Baby High-conflict

Enemy soldiers have taken over your village. They have orders to kill all remaining civilians. You and some of your townspeople have sought refuge in the cellar of a large house. Outside you hear the voices of soldiers who have come to search the house for valuables. Your baby begins to cry loudly. You cover his mouth to block the sound. If you remove your hand from his mouth his crying will summon the attention of the soldiers who will kill you, your child, and the others hiding out in the cellar. To save yourself and the others you must smother your child to death.

How morally acceptable is it to smother your child in order to save yourself and the other townspeople?

Would you smother your child in order to save yourself and the other townspeople?

9. Plane Crash Low-conflict

Your plane has crashed in the Himalayas. The only survivors are yourself, another man, and a young boy. The three of you travel for days, battling extreme cold and wind. Your only chance at survival is to find your way to small a village on the other side of the mountain, several days away. The boy has a broken leg and cannot move very quickly. His chances of surviving the journey are essentially zero. Without food, you and the other man will probably die as well. The other man suggests that you sacrifice the boy and eat his remains over the next few days.

How morally acceptable is it to kill this boy so that you and the other man may survive your journey to safety?

Would you kill this boy so that you and the other man may survive your journey to safety?

10. Lifeboat 2 High-conflict

You are on a cruise ship when there is a fire on board, and the ship has to be abandoned. The lifeboats are carrying many more people than they were designed to carry. The lifeboat you're in is sitting dangerously low in the water—a few inches lower and it will sink. The seas start to get rough, and the boat begins to fill with water. If nothing is done it will sink before the rescue boats arrive and everyone on board will die. However, there is an injured person who will not survive in any case. If you throw that person overboard the boat will stay afloat and the remaining passengers will be saved.

How morally acceptable is it to throw this person overboard in order to save the lives of the remaining passengers?

Would you throw this person overboard in order to save the lives of the remaining passengers?

11. Preventing the Spread 2 High-conflict

You are a waiter. You overhear one of your customers say that he is about to go to jail and that in his last forty-eight hours of freedom he plans to infect as many people as possible with HIV. You know him well enough to know that he is telling the truth and that he has access to many potential victims. You happen to know that he has a very strong allergy to poppy seeds. If he eats even one he will go into convulsions and have to be hospitalized. for at least forty-eight hours.

How morally acceptable is it to cause this man to have a serious allergy attack in order to prevent him from spreading HIV?

Would you cause this man to have a serious allergy attack in order to prevent him from spreading HIV?

12. Ecologists High-conflict

You are part of a group of ecologists who live in a remote stretch of jungle. The entire group, which includes eight children, has been taken hostage by a group of paramilitary terrorists. One of the terrorists takes a liking to you. He informs you that his leader intends to kill you and the rest of the hostages the following morning. He is willing to help you and the children escape, but as an act of good faith he wants you to kill one of your fellow hostages whom he does not like. If you refuse his offer, all the hostages including the children and yourself will die. If you accept his offer then the others will die in the morning but you and the eight children will escape.

How morally acceptable is it to kill one of the fellow hostages in order to escape from the terrorists and save the lives of the eight children?

Would you kill one of your fellow hostages in order to escape from the terrorists and save the lives of the eight children?

13. Bomb 2 High-conflict

You are negotiating with a powerful and determined terrorist who is about to set off a bomb in a crowded area. Your one advantage is that you have his teen-age son in your custody. There is only one thing that you can do to stop him from detonating his bomb, which will kill thousands of people if detonated. To stop him, you must contact him over the satellite hook-up that he has established and, in front of the camera, break one of his son's arms and then threaten to break the other one if he does not give himself up.

How morally acceptable is it to break the terrorist's son's arm in order to prevent the terrorist from killing thousands of people with his bomb?

Would you break the terrorist's son's arm in order to prevent the terrorist from killing thousands of people with his bomb?

14. Submarine High-conflict

You are the captain of a military submarine travelling underneath a large iceberg. An onboard explosion has caused you to lose most of your oxygen supply and has injured one of your crew who is quickly losing blood. The injured crew member is going to die from his wounds no matter what happens. The remaining oxygen is not sufficient for the entire crew to make it to the surface. The only way to save the other crew members is to shoot dead the injured crew member so that there will be just enough oxygen for the rest of the crew to survive.

How morally acceptable is it to kill the fatally injured crew member in order to save the lives of the remaining crew members?

Would you kill the fatally injured crew member in order to save the lives of the remaining crew members?

15. Lawrence of Arabia High-conflict

You are the leader of a small army that consists of warriors from two tribes, the hill tribe and the river tribe. You belong to neither tribe. During the night a hill tribesman got into an argument with a river tribesman and murdered him. The river tribe will attack the hill tribe unless the murderer is put to death, but the hill tribe refuses to kill one of its own warriors. The only way for you to avoid a war between the two tribes that will costs hundreds of lives is to publicly execute the murderer by cutting off is head with your sword.

How morally acceptable is it to cut off this man's head in order to prevent the two tribes from fighting a war that will cost hundreds of lives?

Would you cut off this man's head in order to prevent the two tribes from fighting a war that will cost hundreds of lives?

16. Sophie's Choice High-conflict

It is wartime and you and your two children, ages eight and five, are living in a territory that has been occupied by the enemy. At the enemy's headquarters is a doctor who performs painful experiments on humans that inevitably lead to death. He intends to perform experiments on one of your children, but he will allow you to choose which of your children will be experimented upon. You have twenty-four hours to bring one of your children to his laboratory. If you refuse to bring one of your children to his laboratory he will find them both and experiment on both of them.

How morally acceptable is it to bring one of your children to the laboratory in order to avoid having them both die?

Would you bring one of your children to the laboratory in order to avoid having them both die?

17. Sacrifice Mean High-conflict

You, your husband, and your four children are crossing a mountain range on your return journey to your homeland. You have inadvertently set up camp on a local clan's sacred burial ground. The leader of the clan says that according to the local laws, you and your family must be put to death. However, he will let yourself, your husband, and your three other children live if you yourself will kill your oldest son.

How morally acceptable is it to kill your oldest son in order to save your husband and your other three children?

Would you kill your oldest son in order to save your husband and your other three children?

18. Vitamins High-conflict

You are the leader of a mountaineering expedition that is stranded in the wilderness. Your expedition includes a family of six that has a genetically caused vitamin deficiency. A few people's kidneys contain large amounts of this vitamin. There is one such person in your party. The only way to save the lives of the six members of this family is to remove one of this man's kidneys so that the necessary vitamins may be extracted from it. The man will not die if

you do this, but his health will be compromised. The man is opposed to this plan, but you have the power to do as you see fit.

How morally acceptable is it to forcibly remove this man's kidney in order to save the lives of the six vitamin-deficient people?

Would you forcibly remove this man's kidney in order to save the lives of the six vitamin-deficient people?

19. Vaccine Test High-conflict

A viral epidemic has spread across the globe killing millions of people. You have developed two substances in your home laboratory. You know that one of them is a vaccine, but you don't know which one. You also know that the other one is deadly. Once you figure out which substance is the vaccine you can use it to save millions of lives. You have with you two people who are under your care, and the only way to identify the vaccine is to inject each of these people with one of the two substances. One person will live, the other will die, and you will be able to start saving lives with your vaccine.

How morally acceptable is it to kill one of these people with a deadly injection in order to identify a vaccine that will save millions of lives?

Would you kill one of these people with a deadly injection in order to identify a vaccine that will save millions of lives?

20. Euthanasia High-conflict

You are the leader of a small group of soldiers. You are on your way back from a completed mission deep in enemy territory when one of your men has stepped in trap that has been set by the enemy and is badly injured. The trap is connected to a radio device that by now has alerted the enemy to your presence. They will soon be on their way. If the enemy finds your injured man they will torture him and kill him. He begs you not to leave him behind, but if you try to take him with you your entire group will be captured. The only way to prevent this injured soldier from being tortured is to shoot him yourself.

How morally acceptable is it to shoot this soldier in order to prevent him from being tortured by the enemy?

Would you shoot this soldier in order to prevent him from being tortured by the enemy?

Appendix 3.1 Feeling thermometer

APPENDIXES

The following questions concern your feelings towards different groups. What are your feelings towards the following groups? Please rate your feelings towards the following groups on a thermometer that runs from zero (0) to a hundred (100) degrees. The higher the number, the warmer or more favourable you feel towards the members of these groups. The lower the number, the colder or less favourable you feel. If you feel neither warm nor cold towards members of these groups, rate them at 50.

1. What are your feelings towards Muslims?

0º	10 º	20 º	30 º	40 º	50 º	60 º	70 º	80 º	90 º	100 º
<UNFAVOURABLE (-)>						<FAVOURABLE (+)>				

2. What are your feelings towards white British people?

0º	10 º	20 º	30 º	40 º	50 º	60 º	70 º	80 º	90 º	100 º
<UNFAVOURABLE (-)>						<FAVOURABLE (+)>				

3. What are your feelings towards asylum seekers?

0º	10 º	20 º	30 º	40 º	50 º	60 º	70 º	80 º	90 º	100 º
<UNFAVOURABLE (-)>						<FAVOURABLE (+)>				

4. What are your feelings towards black British people?

0º	10 º	20 º	30 º	40 º	50 º	60 º	70 º	80 º	90 º	100 º
<UNFAVOURABLE (-)>						<FAVOURABLE (+)>				

5. What are your feelings lesbians?

0º	10 º	20 º	30 º	40 º	50 º	60 º	70 º	80 º	90 º	100 º
<UNFAVOURABLE (-)>						<FAVOURABLE (+)>				

6. What are your feelings towards Christians?

0º	10 º	20 º	30 º	40 º	50 º	60 º	70 º	80 º	90 º	100 º
<UNFAVOURABLE (-)>						<FAVOURABLE (+)>				

7. What are your feelings towards Drug addicts?

0º	10 º	20 º	30 º	40 º	50 º	60 º	70 º	80 º	90 º	100 º
<UNFAVOURABLE (-)>						<FAVOURABLE (+)>				

Appendix 3.2

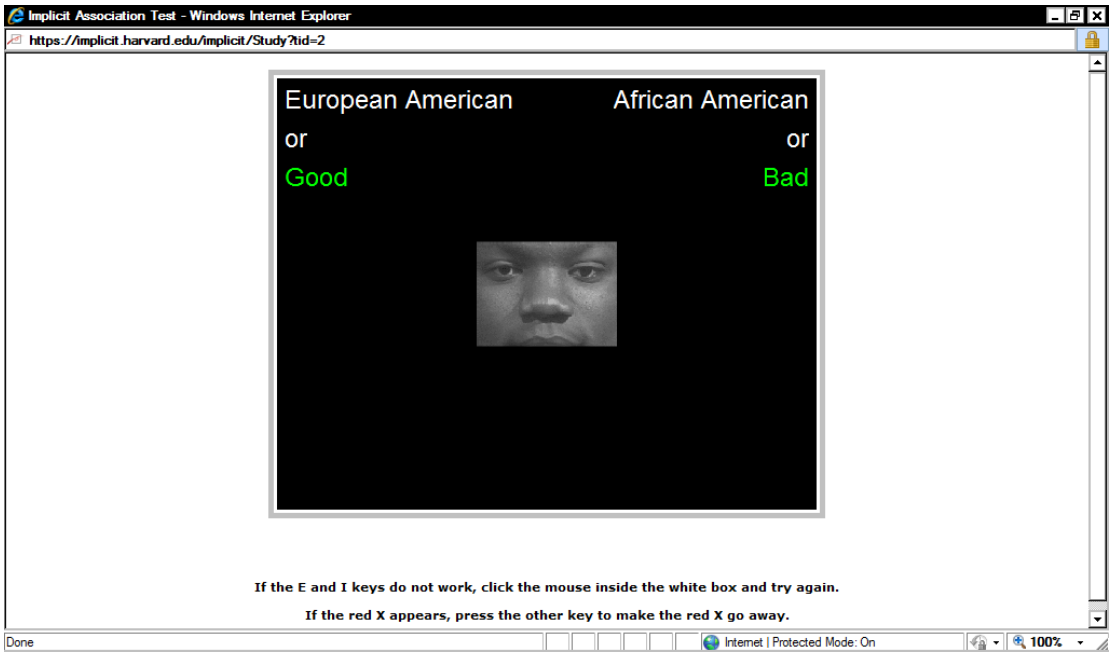
IAT

APPENDIXES

Example picture from an American IAT; I used:

Good, Bad,

Black and White European:



Arrangement of the IAT

Block	**Number of trials**	**Items assigned to the left key**	**Items assigned to the right key**	**Description**
1	20	Positive words	Negative words	/
2	20	White Faces	Black Faces	/
3	20	Positive Words and White Faces	Negative Words and Black Faces	Congruent 1
4	20	Positive words and White Faces	Negative Words and Black Faces	Congruent 2
5	20	Negative Words	Positive Words	/
6	20	Negative Words and White Faces	Positive Words and Black Faces	Incongruent 1
7	20	Negative Words and White Faces	Positive Words and Black Faces	Incongruent 2

Appendix 4.1

Additional moral dilemmas used in study 3 and 4 (reboxetine)

Moore – inevitable/personal

RESCUE 911

You are the sole paramedic riding on a rescue helicopter, responding to a devastating flood. You have rescued several critically injured people and you have been treating them to keep them alive. Suddenly, the pilot notifies you that there has been an engine malfunction and the helicopter can no longer support the weight of you, the pilot, and all the injured people on board. If the helicopter crashes, it will kill everyone on board including you, the pilot, and the injured people that you have rescued. In order to avoid a crash that will kill everyone on the helicopter, you realize that you must lighten the load enough to keep the helicopter aloft. Because all of the equipment is bolted down, and you are needed by the injured people, the only way to do this is to throw one of the injured people off the helicopter. This will lighten the load enough to keep the helicopter in the air but will cause the death of the person thrown off.

How morally acceptable is it to kill this injured person in order to save yourself and everyone else on board?

SPACE STATION

You are an engineer on the international space station, in orbit around the Earth. Suddenly, a fire breaks out in the cargo bay. The automatic fire safety system will open the outer door of the cargo bay, letting the oxygen out of the bay and thus putting out the fire. The automatic system only works when the inner portal to the rest of the station has been sealed. One member of the crew, a mechanic in the cargo bay, has put on half of his bulky space suit when

the fire begins. He runs to the portal to climb through to safety, but the portal is too narrow to fit through while wearing a space suit. You realize that if he tries to climb through, he will get stuck and the fire will spread through the rest of the station because the safety system will not operate with the portal open. There is no time for him to take off the suit before the fire spreads. The only way you can prevent the spread of the fire, and save your life and the rest of the crew, is to push the mechanic back through the portal and into the cargo bay. This way, the safety system will seal the door and decompress the cargo bay, but it will also suck the mechanic into space and kill him.

How morally acceptable is it to push the mechanic back through the portal, and into space, in order to save yourself and the rest of the crew?

NUCLEAR REACTOR

You are the inspector of a nuclear power plant that you suspect has not met its safety requirements. The plant foreman and you are touring the facility when one of the nuclear fuel rods overheats. The emergency coolant system fails to activate, and a chain reaction is about to begin which will result in a nuclear meltdown. This will release lethal radiation into the nearby town, killing thousands of people. You realize that the only way to stop the meltdown is to push the foreman into the fuel rod assembly. This will remove just enough heat energy from the rod assembly to prevent the nuclear chain reaction. However, it will also incinerate the foreman instantly.

How morally acceptable is it to push and kill the foreman in order to save yourself and the nearby town?

CINDERBLOCK

You are the explosives expert for a company that has been hired to demolish a skyscraper. You are examining the last of the explosive charges when you notice a teenager below who is about to accidentally detonate one of the charges out of sequence. This explosion will result in the building's uncontrolled collapse onto you, the teenager, and the crowd of spectators. The teenager is several floors below you and cannot hear you because of the loud demolition noise. You realize that the only way to stop the teenager from detonating the charge is to drop a heavy cinderblock on his head. This will crush his skull and kill him almost instantly but will prevent the out-of-sequence explosion.

How morally acceptable is it to kill the teenager in order to save yourself and the crowd of spectators?

CLIFFHANGER

You are a construction worker. You and your crew are high on a scaffold, working on a skyscraper. Suddenly, the scaffolding partially collapses. You and several others are hanging on to a dangling crossbar, but it cannot hold all of your weight. The worker next to you slips off the crossbar and grabs a hold of your one free arm. However, you realize that the entire structure is about to give way. The only way to avoid you and everyone else falling to your deaths is to repeatedly kick your co-worker in the stomach and chest until he lets go of your hand and falls to his certain death. This will remove just enough weight that the rest of you can make it to safety before the scaffold collapses.

How morally acceptable is it to kill your co-worker in order to save yourself and the rest of the crew?

+ More

Transplant Low-conflict

You are a doctor. You have ten patients, each of whom is about to die due to a failing organ of some kind. You have another patient who is healthy. The only way that you can save the lives of the first ten patients is to transplant five of this young man's organs (against his will) into the bodies of the other ten patients. If you do this, the young man will die, but the other ten patients will live.

How morally acceptable is it to perform this transplant in order to save ten of the patients?

Footbridge High-conflict

A runaway trolley is heading down the tracks toward ten workmen who will be killed if the trolley proceeds on its present course. You are on a footbridge over the tracks, in between the approaching trolley and the ten workmen. Next to you on this footbridge is a stranger who happens to be very large. The only way to save the lives of the ten workmen is to push this stranger off the bridge and onto the tracks below where his large body will stop the trolley. The stranger will die if you do this, but the ten workmen will be saved.

How morally acceptable is it to push the stranger on to the tracks in order to save the ten workmen?

Ecologists High-conflict

You are part of a group of ecologists who live in a remote stretch of jungle. The entire group, which includes 16 children, has been taken hostage by a group of paramilitary terrorists. One of the terrorists takes a liking to you. He informs you that his leader intends to kill you and the rest of the hostages the following morning. He is willing to help you and the children escape, but as an act of good faith he wants you to kill one of your fellow hostages whom he does not like. If you refuse his offer, all the hostages including the children and yourself will die. If you accept his offer then the others will die in the morning but you and the 16 children will escape.

How morally acceptable is it to kill one of the fellow hostages in order to escape from the terrorists and save the lives of the eight children?

Sacrifice Mean

You, your husband, and your four children, and 7 others are crossing a mountain range on your return journey to your homeland. You have inadvertently set up camp on a local clan's sacred burial ground. The leader of the clan says that according to the local laws, you and your family and all the other people must be put to death. However, he will let yourself, your husband, your three other children, and the others live if you yourself will kill your oldest son.

How morally acceptable is it to kill your oldest son in order to save your husband and your other three children, and the 7 other people?

Vitamins High-conflict

You are the leader of a mountaineering expedition that is stranded in the wilderness. Your expedition includes 2 families of six that have a genetically caused vitamin deficiency. A few people's kidneys contain large amounts of this vitamin. There is one such person in your party. The only way to save the lives of the two family is to remove one of this man's kidneys so that the necessary vitamins may be extracted from it. The man will not die if you do this, but his health will be compromised. The man is opposed to this plan, but you have the power to do as you see fit.

How morally acceptable is it to forcibly remove this man's kidney in order to save the lives of the twelve vitamin-deficient people?

Lying Dilemmas

White Lie 1

A friend of yours, who gives great weight to the opinion of Fred, wants to know what Fred thinks of him and will believe whatever you tell him. In fact, Fred is not worthy of this confidence, indeed, is sloppy and prejudiced in his opinions. Fred despises your friend and your friend would be devastated to find this out, but will only find it out if you tell him. It would do enormous good for his self confidence and self esteem if he thought that Fred esteemed him highly.

How morally acceptable is it to tell him that Fred despises him?

White Lie 2

A young friend of yours always greatly admired his uncle, who has just died and whom you knew well. At the funeral the nephew asks you to tell him what his uncle really thought of him. As a matter of fact, his uncle disliked him and the young man would be devastated to find this out. However, his uncle was superficial and spiteful in his opinions of people and was not worthy of the young man's esteem. It would do much good for the young man's confidence and self esteem if he thought that his uncle thought well of him.

How morally acceptable is it to tell your friend that his uncle disliked him?

White Lie 3

The husband of your close friend Jane told you that he had a secret romantic involvement with another woman four years ago but would never want to do so again, since his marriage means so much to him. On a night out with Jane she mentions that she was worried about her marriage four years ago. Jane goes on to say that her marriage is immensely important to her and that if her husband was ever unfaithful it would destroy the marriage because she would never be able to trust him again. She asks whether you've ever heard anything to suggest her husband isn't faithful.

How morally acceptable is it to tell Jane that her husband had an affair?

White Lie 4

Last year the government has banned the works of a particular author on the grounds that they are sexist and racist. Your neighbour has always been a fan of that author and you know he has

hidden his collection of that author's books somewhere in his house. The police are searching his house. You know that they are hidden behind a false wall in his attic. You have heard the police searching his house all day and they have now come round and demand that you tell them where the books are. If they find the books your neighbour will be convicted and will be demoted at work. If you lie to them they will never find his books.

How morally acceptable is it to tell the truth about your neighbour?

White Lie 5

You are on friendly terms with your two neighbors, Jeff and Bob. Unfortunately, they are both hot-headed and hate each other. The tension between them has been growing recently. The other day, you've seen Bob carelessly dropped some trash near Jeff's yard. Jeff has just knocked on your door, evidently angry, and asked you if it was Bob who left the trash. If you tell him the truth, you know he'll head straight to Jeff's house and they'll have a violent fight. If you lie and tell him that it was you who accidentally dropped the trash Bob will soon forget about the whole thing.

How morally acceptable is it to tell him Bob left the trash?

Appendix 4.2

Semantic differential explicit prejudice measure

Describe how you feel about black people in general

Cold	(1)	(2)	(3)	(4)	(5)	(6)	(7)	**Warm**
Negative	(1)	(2)	(3)	(4)	(5)	(6)	(7)	**Positive**
Friendly	(1)	(2)	(3)	(4)	(5)	(6)	(7)	**Hostile**
Suspicious	(1)	(2)	(3)	(4)	(5)	(6)	(7)	**Trusting**
Respect	(1)	(2)	(3)	(4)	(5)	(6)	(7)	**Contempt**
Admiration	(1)	(2)	(3)	(4)	(5)	(6)	(7)	**Disgust**