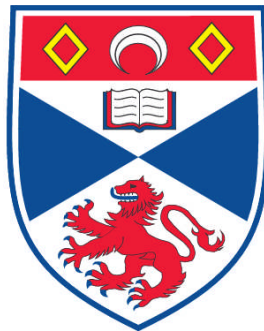


**WHAT DOES IT MEAN TO EXPERIENCE PAEDIATRIC
DEPRESSION?: THE ETHICS OF MENTAL HEALTH DIAGNOSIS
AND TREATMENT IN CHILDREN AND ADOLESCENTS**

Molly Deacutis

**A Thesis Submitted for the Degree of MPhil
at the
University of St. Andrews**



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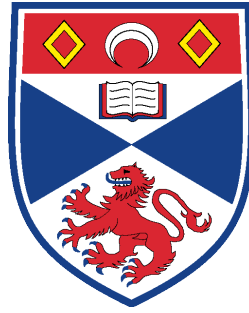
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University
of
St Andrews

School of Biology

MPhil Thesis

What Does It Mean to Experience Paediatric
Depression?: The Ethics of Mental Health Diagnosis
and Treatment in Children and Adolescents

By

Molly Deacutis

July 2011

Declarations

I, Molly Deacutis, hereby certify that this thesis, which is approximately 37,000 words in length, has been written by me, that it is the record of work carried out by me and that it has not been submitted in any previous application for a higher degree.

I was admitted as a research student in September 2010 and as a candidate for the degree of MPhil in September 2010; the higher study for which this is a record was carried out in the University of St Andrews between 2010 and 2011.

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Abstract

This thesis explores the ethics of mental health diagnosis and treatment in children and adolescents through a collection of different perspectives based on literature analysis and interviews with practicing clinicians. Compared to other medical fields, paediatric psychiatry is considerably novel; it has only recently become a medical specialty and differs from other medicine by involving both biological and psychological aspects of care. Recently, human brain development has become better understood, but the effect of mental illness on the trajectory of development is only just beginning to be studied. Despite this limited understanding, children who may not have been diagnosed for psychiatric disorders in the past are increasingly receiving off-label prescription treatments. This trend may be due to improved sensitivity of diagnostic practices as well as the medicalisation of normal, classifying previously healthy borderline behaviours as pathological. What are the implications of increasing medicalisation? How are child-specific diagnoses and treatment plans determined? I focus on identity development in young people with mental disorders, specifically depression, and try to explain the effects of labelling and medication on that development. Also the physiological impact of psychopathology and psychotropic treatment on neurodevelopment is examined, as well as the lack of long-term clinical data for drug treatment in children. Though the key source material has been from literature in the US and UK, the thesis broadens to an international perspective with a global look at the relationship between culture and paediatric psychiatry practices. Finally, mental health care professionals were interviewed to provide a clinical perspective to supplement the literature analysis. By drawing historical, philosophical, psychological, biological, cultural, and professional perspectives together in this novel way, ethical considerations necessary in the psychiatric care of paediatric patients are given a more thorough understanding, and a framework for assessing these considerations is presented through a focused interdisciplinary lens.

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CHAPTER 1

Introduction

In Western society, the practice of medically diagnosing and treating children for psychiatric illness is rapidly growing. Not only are more diagnoses being defined and extended to the paediatric population, but the rate of development of new diagnoses is being outpaced by the increasing rate at which children are being diagnosed and treated within psychiatry. While research has provided significant understanding of the human brain, the interplay between psychology and biology, particularly during development, remains largely unclear, though technology has allowed doctors some level of psychological manipulation through biological treatments. Although adult psychiatry continues to evolve as a relatively new medical science, it is supported by well over a century of study and decades of clinical drug trials. On the other hand, paediatric psychiatry is a considerably more recent and less studied field, and lacks comparable data evidence provided in adult practice. There is extensive research discussing specific elements of ethical concerns in paediatric psychiatry, including what data *is* available, the issue with treating despite lack of data and the future of paediatric psychiatry (e.g. Vasa, Carlino & Pine, 2006; Moreno et al., 2007; Alacqua et al., 2008; Parens & Johnston, 2011), but no one study that pulls all this together to investigate the overall context and implications of paediatric psychiatry.

In one literature review, Lakhan and Hagger-Johnson (2007) highlight five major points of interest when treating children with psychotropic medication. Firstly, though the human brain continues to change over an entire lifetime, the developing brain is changing more rapidly than the adult brain; this implies not only that children and adolescents may respond differently to drug treatments than adults do, but it also suggests that it may be more ethically challenging to conduct research to study paediatric brain-drug interactions because the immature brain is more susceptible to insult. Secondly, children and adolescents are at

high risk for developing depression and other mood disorders due to the combination of experiencing increasingly stressful events as they age and possessing a particularly malleable identity as they develop a sense of self-understanding. Thirdly, the symptoms and extent to which these symptoms are considered meaningful in terms of the impact it has on an individual is different in children from that in adults; hence, the same disorder may present differently depending on the age of the patient. Fourthly, psychotropic drug dosages should not simply be lowered for children, based on age and body size; the difference between metabolic rate in children versus adults and unknown long term effects on neurodevelopment must also be considered. Lastly, despite the tendency to rely on psychotropic treatment, it is important to remember that there are other psychiatric treatments that have been proven effective in the paediatric population, not only drugs. Cognitive behavioural therapy (CBT) and parent training are examples of alternative interventions.

In order to draw together a picture of current paediatric psychiatry, this thesis will illustrate the major ethical concerns in the field by focusing on depression to demonstrate the issues as they appear in the child and adolescent population. Before exploring this disorder in the context of paediatrics, however, the implications of modern medicine's understanding of adult depression should be discussed. Adult psychiatry also faces a number of issues similar to those which affect paediatric treatment. Specifically addressing depression in adults, recent literature calls attention to the impact the disorder and treatment has on personal experience, the growing reliance on psychotropic medication, neglect of context, and medicalisation of normal (e.g. Elliott, 2000; Healy, 2000; Parens, 2004). Previously, melancholic individuals experiencing depression appeared to possess a superior virtue and ability to question and understand human life, a virtue which has faded in modernity; as Kramer (2000, p. 17) eloquently notes,

I have asked why we are no longer charmed by suicidal
melancholics—Goethe's Werther or Chateaubriand's Rene

or Chekov's Ivanov. Because we see major depression and affectively driven personality disorders as medically pathologic, what once exemplified authenticity now looks like immaturity or illness—as if the romantic writers had made a category error.

Yet, correlated with the depth of depressive experience and its associated insight, a number of these affected individuals became influential cultural, social, and political leaders throughout history (Kramer, 2000; Ghaemi, 2003), e.g. George Washington, Ulysses S. Grant, and Abraham Lincoln (Ghaemi, 2003). However, with the increased awareness of depression as a disorder and the availability of effective psychotropic treatment, Western society shows an increasing trend toward medicating depressed individuals as the go-to treatment approach, while discounting the experience and context that gives rise to and results from depression (Healy, 1997). Kramer (2000) argues that this trend reflects society's attempt to mainstream human experience, treating who people are and human authenticity as a disease that needs to be cured. Rather than viewing depression as a different version of normal or an extreme response to significant life stress and grief, what used to be considered within normal life experience has become more often medically diagnosed as a disorder and treated, particularly through psychopharmacology (Horwitz & Wakefield, 2007). This may not be a *bad* trend, but it does question the value of experience and prompts questions of how such practices may impact both individuals and the larger society.

Led by a series of questions, this study involves an interdisciplinary analysis of the treatment of depression in the young population in the US and UK by addressing six key aspects: historical background, the concept and ethics of medicalisation¹, identity development and psychological implications of treatment, physiological implications of treatment, cultural influences, and professional opinions. Considering the historical perspective in the form of a literature review, the development of the psychiatric diagnosis

¹ 'Medicalisation' refers to the shift toward medically diagnosing previously 'normal' experience/behaviour, and while the term itself does not imply medication, it does often lead to medication treatment.

and its extension to the paediatric population will be discussed; particular attention will be given to emerging treatment and prescription trends over the past few decades. The concept of psychiatric diagnosis, along with its associated drug treatment, is considerably novel and it is only recently that both have been broadened to include children and adolescents. Next, the section on medicalisation will consist of an examination of the purpose of diagnosis and treatment, an evaluation of what is normal, and a comparative analysis of neurostimulant and antidepressant use for neuroenhancement purposes. As the definition of normal narrows, more children are receiving psychiatric treatment than ever before. Further, there has been much debate over the use of neurostimulants not only for treatment of ADHD but also cognitive enhancement. Based on this trend of neurostimulant enhancement in children and the practice of Prozac enhancement in adults, it may be likely that similar issues are on the rise for antidepressant use in arguably healthy children in order to attain a desirable effect, including decreased anxiety, increased confidence, or less negative temperament, for instance. Psychotropic treatment for both ADHD and depression, among other psychiatric disorders, raise concerns about the identity and concept of self as young individuals may integrate their disorder and treatment into their understanding of themselves. The psychological implications of depression treatment will be ethically assessed through a discussion of the available literature, taking into account the development of identity, experience of the disorder and the effects of treatment on the individual. Additionally, a similar analysis of known physiological effects will follow. This perspective will investigate the interaction between neurodevelopment, disorder, and treatment. As policy is a significant factor in protecting the rights and safety of vulnerable populations, including paediatrics, and driving the future of developmental research, an overview of the relevant legislation will be summarised. It has also been observed that culture and social influences play a large part in the treatment available and sought after, particularly for mental health; such influences will

be investigated as they pertain to the treatment of paediatric depression. A comparison of a range of international literature will be presented, and the implications of Western practices will be analysed within this international context. To conclude the study, professional opinions are sought in order to speak more directly to the issues presented in this thesis as they appear in clinical practice by conducting semi-structured interviews with a small sample of paediatric mental healthcare professionals.

CHAPTER 2

What is the context of paediatric depression in psychiatry?: A historical perspective

2.1 How did paediatric psychiatry develop?

The concept of paediatric depression is a recent development in the field of psychiatry. Compared to other fields, psychiatry itself is very young. Further, within this specialty recognizing the paediatric population separately from adults is even more novel. Child psychiatry only became an official subspecialty of psychiatry in 1959 (Chess & Hassibi, 1978). While children have been incorporated into mental health care schemes since the turn of the twentieth century, until this point children were simply treated for adult-centric disorders. No consideration was given to the possibility that immature minds perceive and experience psychiatric illness differently than adult minds. Originally, professional attention toward mental health specific to the paediatric population came only as a means to help juvenile delinquents, the first recognized program being in 1909 in Chicago (Chess & Hassibi, 1978).

While stages of child development have been acknowledged, a disconnect appears between this awareness and the determination to apply adult diagnoses in a similar manner to such a dissimilar population. Without further investigation, it is easy to assume adult diagnoses remain applicable. However, when brain development is considered, significant differences in the child brain beg the question, are the set diagnostic criteria and even the diagnoses themselves appropriate? For the adult population, valid diagnoses may be attributed to individuals based on relatively objective criteria. Even later in life psychiatric disorders are difficult to define precisely for each individual because no two people have exactly the same experiences or mental processes, but through adults' matured comprehensive and communicative abilities, experiences may be roughly generalized by

defined disorders. Yet, diagnoses themselves are continually evolving, so there will always be a level of subjectivity. Turning to a young population then, applying diagnostic criteria must be even more subjective because the degree of significance that any one experience will have for a given child will be much more variable due to the limited life experiences and comprehension. As such, diagnostic criteria must be approached differently when dealing with children.

2.2 How are children and adolescents incorporated into their own medical treatment?

Before investigating the application of diagnosis and effects of treatment and medication on this population, their needs and integration into the medical system require an introduction and understanding. Paediatric care is unique in that it incorporates not only the physician and immediate child patient, but also includes parents as ‘patients’ because they are affected by and consent to treatment given to their child. Specifically in the US, if the patient is under 18 years of age then treatment requires parental consent (with few exceptional circumstances), so parents must be included in clinical visits and receive all pertinent information.

Taylor et al. (2010) conducted a qualitative study in the UK interviewing 20 families about their personal feelings about their paediatric consults. The purpose of this study was to investigate the attitudes toward the inclusion of the paediatric patient in the management of their own care. There were a number of factors deemed important in determining child involvement levels that were mentioned by participants, including age, maturity, communication skills of child, comfort levels of child, gender, cognitive ability, confidence, family dynamics, doctor’s judgment, and illness severity. Involvement was encouraged in order to provide the best service, but there was also a counter to such involvement in hopes of protecting the child patient; typically, families looked to the doctors to decide the extent to

which the child should be included. Including the child patient in his or her treatment was viewed as the only means of fully communicating the illness that caused the child (and parent) to seek help. In fact, the researchers suggested consulting adolescent patients both with and without their parents present to both aid treatment determination and give the patient more responsibility for their own health.

Despite the benefits of including the child in the communication during consultation, a child patient is not an equal player in the clinical setting and continues to contribute less to his or her own care, with a number of identified barriers. Often the patient, both child and parent, are afraid of taking up too much of the doctor's time, wanting to use as little time as possible, and fear that the clinical process would only be slowed down by a child trying to articulate his or her condition. Concern was noted by a minority of families that the doctor should consult the parent first. This would allow the parent to understand the diagnosis before including the child in order to better support and protect the child, and to alleviate some responsibility from the child of making difficult decisions with serious long term effects. Also, 'doctor knows best' tends to shy away the child patient, and to an extent the parent, from involvement, assuming the doctor is the expert and, thus, does not need the help of the patient in determining diagnosis and treatment. Ultimately, most families felt comfortable leaving the decision to the doctor to choose how best to include the child patient. It should also be noted that child involvement in their own care has been increasing over the past few generations, marking a social trend, and has been reflected in medical practice to enhance this trend (Taylor et al., 2010).

2.3 What does it mean to have the diagnosis of depression?

Firstly, what does it mean to have a diagnosis? What is the purpose of diagnosing a patient, whether it be for depression or any other disorder? There are a number of

perspectives necessary to consider in order to fully answer these questions. In the most general sense, a diagnosis provides a label. For the physician, this offers a lead on the appropriate treatment plan. Particularly in the US, this allows third party insurance claims to subsidize the cost of care. For a given diagnosis, a patient's insurance coverage will pay for specific amounts and types of care, for example consults, tests, and prescriptions, which would otherwise be at the expense of the patient without an identified diagnosis. Additionally, disability services or accommodations may be provided if the diagnosis calls for such facilities. In other healthcare systems, such as the NHS in the UK, diagnosis is less vital to healthcare access, but may be necessary to obtain disability services or to create an effective treatment plan.

The diagnosis may be equally important for the patients themselves. Putting a label on their experiences helps some individuals recognize what may otherwise be an overwhelming and isolating complexity of feelings. It provides something real and definitive that they can identify with, albeit something abstract. Through the identification of a diagnosis, patients are also able to find support and create a community with others who share similar experiences. Due to its influence not only on treatment but also a patient's own identity, it is crucial to consider a diagnosis thoroughly before applying such a heavy label.

Before addressing its application to the paediatric population, it is important to understand the diagnosis as it is written. Generally, diagnoses are made based using either the Diagnostic Statistical Manual of Mental Disorders (DSM) or by the International Statistical Classification of Diseases and Related Health Problems (ICD); currently, diagnoses are based on the DSM-IV (1994) or ICD-10 (1992), both of which are in the revision stages for new editions to be published shortly. While the two classification tools are separate, they are not competing theories. The ICD, published by the World Health Organization (WHO), is meant to be more generalized to the entire (Western) population,

whereas the American Psychiatric Association's DSM is more specific and sensitive toward American culture and social understanding.

In the ICD, the diagnosis of depression is broken into two categories, Recurrent Depressive Disorder and Depressive Episode, within which there are four subcategories: mild (with and without somatic symptoms), moderate (with and without somatic symptoms), severe without psychotic symptoms, and severe with psychotic symptoms (see Appendix A for full ICD 10 diagnostic criteria). As stated under the Depressive Episode diagnosis, 'Differentiation between mild, moderate, and severe depressive episodes rests upon a complicated judgment that involves the number, type, and severity of symptoms present' (IMH, 2009). In other words, the authors are calling attention to the subjectivity of this classification method. Further, the mention of diagnosing adolescents is specified as commonly showing an atypical presentation. If this is the case, then such a presentation will not likely fit the criteria marked out by the authors, making the diagnosis even more subjective.

Similarly, the DSM divides the diagnosis of Major Depressive Disorder into either a single Major Depressive Episode or recurrent Major Depressive Episodes (see Appendix B for full DSM IV diagnostic criteria). Depression is diagnosed given the presence of at least five of the listed symptoms, regardless of severity, which is later listed as a specifier. With this minimum number of symptoms required for diagnosis, however, there is less flexibility in the DSM classification than the ICD, which adjusts the severity based partially on number of symptoms present. The DSM gives attention to paediatric diagnosing with respect to two of the nine listed symptoms. First, there is a note following depressed mood indicating that this symptom may be perceived as irritable mood in children and adolescents. Second, significant weight and/or appetite changes may also be observed as a child's failure to meet expected weight gains, a variable not relevant to adult depression. Are these the atypical

features in paediatric depression that the ICD is alluding to? Or is the DSM missing a catch-all clarification that paediatric depression may present differently, not only in the two specified symptoms?

Regardless if a physician is trying to diagnose a child, adolescent, or adult, are the diagnoses outlined above adequate? According to Saito et al. (2010), following a comparison of the two diagnostic systems, 'the ICD-10 seems more sensitive to the mild range of the depressive continuum, while the DSM-IV seems to be more sensitive to the moderate and severe ranges' (p. 220). Still, when using the DSM and less so the ICD, ticking off a set number of symptoms seems to be an overly simplified method of diagnosing. If psychiatric disorders are acknowledged as highly subjective, it is counterintuitive to use strict numbers as a measure. Indeed, the line separating 'disordered' and 'normal' individuals needs to be drawn somewhere, which is a markedly difficult task requiring classification of something so intangible and subject to constant amendment and redefinition. Diagnosis as a tool can only be as effective as its measure. Despite lacking the most accurate measure of psychiatric illness, a diagnosis should not be discounted. As described above, the diagnosis does hold significance both to the physician and the patient. However, while the care for most medical disorders benefits from diagnosing as a means to outline the treatment plan, perhaps those approaching psychiatric disorders should consider the treatment plan first in order to determine a suitable diagnosis.

In theory, the diagnosis is made based on the symptoms, so it should match the appropriate treatment plan; yet, the match is not always as clear when treating psychiatric disorders. Compare a testable infection such as streptococcal pharyngitis (strep throat) to a subjective psychiatric diagnosis such as Obsessive Compulsive Disorder (OCD). The physician can say without reasonable doubt that the patient has strep throat based on a positive test for the bacteria causing the infection. With the symptoms and positive test to

support the diagnosis, the physician will prescribe an antibiotic treatment, and most patients would recover in the following days. Of course, there are cases that do not resolve as easily or that take a different course due to variability between individual patients, but such results are unusual and do not discredit the diagnosis overall. On the other hand, a physician can diagnosis OCD based on symptoms exhibited by a patient, and will use this diagnosis in order to develop a treatment plan. However, often patients experience comorbid psychiatric disorders, so there may be other less prominent disorders that are overlooked once the physician directs focus on the specific disorder of OCD. It is also possible that the OCD tendencies exhibited by the patient are a symptom of an even greater disorder, such as a developing psychosis. Particularly with psychological disorders, patients require very specific individualized treatment plans that are not easily directed strictly by diagnosis.

2.4 What does it mean for a child to be ‘depressed’?

Given that both the ICD and DSM note the atypical presentation of depression in children and adolescents, how can depression be identified in this population? The ICD does not clarify what to look for as an ‘atypical presentation,’ which leaves the notion that the diagnosis as stated there is of little use when dealing with the paediatric population. Alternatively, the DSM is slightly more specific about the presentation in children and adolescents, but even so, suggestions made to identify paediatric depression, such as ‘irritable mood,’ are much more difficult to distinguish from normal adolescent behaviour. As stated earlier, depression, in line with other psychiatric disorders, is subjective in nature, and even the same symptoms may have different levels of impact from person to person. Such variation is exaggerated in the paediatric population as this age group is still developing coping mechanisms. Temperament at this age is constantly in flux as young people learn to deal with life in addition to hormonal and other physiological changes occurring. As a result,

some children and adolescents may appear to struggle to cope due to out of control emotional expression, but will naturally overcome these challenges with time. Others may appear to handle life stress with a more agreeable demeanour, but are actually unable to express internal turmoil due to limited juvenile ability to communicate. Typically, the symptoms exhibited in adults are severe enough that a diagnosis of depression is made due to insufficient coping mechanisms necessary for dealing with life stress and/or other biological causes. In children, on the other hand, it is difficult to determine if an individual's lack of appropriate coping mechanisms will develop over time or must be compensated by diagnosis and treatment.

2.5 What are the prescription trends in the paediatric population?

Known for its overmedicated population, the US shows some interesting trends in its treatment of disordered youth. There are a number of papers investigating these trends, one example being Rushton and Whitmire (2001). The authors conducted a study describing paediatric prescription trends in the US from 1992 to 1998, specifically tracing prescriptions of Selective Serotonin Reuptake Inhibitors (SSRIs) and psychostimulants, which are the two most prevalent classes of medication in paediatric psychiatry and are commonly given for depression and ADHD, respectively. This study included children in the North Carolina Medicaid Program between the ages of 1-19, and found that the number of prescriptions filled, number of patients treated, and percentage of children on medication all increased over the decade. The prescription prevalence, which is the number of patients in a specific age group within the sample receiving a prescription, of stimulants in school-aged children (ages 6-14) increased from 4.4% to 9.5% over the seven year study, while that of SSRIs increased from 0.2% to 1.5%. Additionally, the study showed an increase of combining stimulants and SSRIs, which brings up serious concerns due to extreme lack of experimental data in

combining medications. While SSRI treatment was relatively novel in the early 1990s, by 1998 nearly one third of those children included in the study who were taking SSRIs were also prescribed stimulants. Finally, this work also highlights age, sex, and racial differences that require further investigation. While there was a slight increase in the mean age for stimulant prescriptions from 8.5 to 9.1 years old, that for SSRI prescriptions dropped from 14.9 to 13.1 years old. Gender differences in prevalence appear to be converging, though male stimulant prescriptions remain noticeably, and expectedly, higher than that for females. More concerning are the racial differences between prescription recipients. Despite not being the majority of Medicaid patients, the white population notably received the majority of prescriptions for both stimulants and SSRIs; is this an indication of different mental health risks in different racial backgrounds, different values/stigma for seeking care, or an issue of access to care? Further study is required to untangle this trend (Rushton & Whitmire, 2001).

A particular concern has also been the increase in prescriptions for preschoolers, specifically stimulants, because this group is faced with such high off-label use. Zito et al. (2000) published a now well-known study investigating prescription trends in 2- to 4-year-olds through the years of 1991 to 1995 in a sample including multiple state Medicaid programs and a health maintenance organization (HMO) to gather data across age, gender, geographic location, and varying health care system groups. Findings were similar to those found for older children and young adolescents, with significant increases in the number of prescriptions during the study period in the early 1990s. These trends are alarming considering the significant lack of data for such young patients, leaving these patients at even greater risk than older children. Preschooler stimulant use was the most prevalent psychotropic treatment in this age population, particularly methylphenidate (Ritalin). The article cites the following possible reasons for the increasing trend in stimulant use:

- (1) a larger pool of eligible youths because of expanded diagnostic criteria for ADHD since 1980; (2) more girls being

treated for ADHD as evidenced by the narrowing of the gender ratio even among preschoolers; (3) greater acceptance of biological treatments for a behavioural disorder; and (4) the expanded role of school and preschool health personnel in identifying medical needs. (Zito et al., 2000, p. 1028)

While all plausible reasons, they also raise more questions and room for possible concern. Expanding the diagnostic criteria allows children to be diagnosed who may not have been treated in the past. To what extent, however, do these newly included children *need* treatment and medication, presuming that they would have previously been considered borderline cases? Diagnosing more girls highlights similar concerns; what is allowing the gender gap to narrow? Is it the expanded diagnosis? Are clinicians better able to recognize symptoms, particularly how they may present differently between genders? Turning to biological treatments for behavioural disorders can be incredibly effective to the patient. At the same time, connections between biology and behaviour, as well as biological mechanisms of these medications themselves, remain widely unknown. While the noted benefits encourage treatment use, such treatments should also be approached with caution. Comparable results were found with antidepressant treatment, which “were the second most commonly prescribed psychotropic class of drugs for preschoolers” (Zito et al., 2000, p. 1028). Tricyclic antidepressants (TCAs) proved to be the most prevalent of this class, but during this period the trend began shifting toward SSRI use (more so in Medicaid groups than HMOs), mirroring previous trends in older populations. In general, differences found between geographic regions as well as health care systems may be attributed to such factors as state policies and access to care, including who is eligible for Medicaid services, training of and assessment by professionals working with children in different regions, and sociocultural variations, including economic, ethnic, and cultural value differences.

As Rey, Walter and Hazell (2000) in Australia point out, preschool prescriptions are a worldwide problem with serious ethical implications. Highlighting six major concerns that arise when treating preschoolers, the authors state:

Firstly, with few exceptions, in most countries these medications are not approved for use in the very young. Secondly, there are very few controlled data showing whether they are effective in this age group. Thirdly, psychiatric diagnoses in preschoolers generally lack validity and reliability [...] Fourthly, there is little knowledge and considerable apprehension about the long-term effect of psychotropics on the developing brain. Fifthly, there are scarce data about the pharmacokinetic and pharmacodynamic characteristics of these drugs in the very young. Finally, rather than placing the best interests of the child first, some practitioners may react to pressure from preschools, childcare services or parents. [...] The problem is magnified if the child is reviewed infrequently, as seems the case for many of those taking stimulants. (Rey, Walter & Hazell, 2000, p. 172)

Over all, these concerns broadly extend to older children and adolescents. Though more safety and efficacy data do exist for older paediatric populations, this knowledge base remains significantly limited. A key issue in the lack of data is due to ethical concern, which creates a ‘vicious cycle’ (Rey, Walter & Hazell, 2000, p. 173). Treatments are often prescribed off-label due to the lack of research done for this particular population. However, carrying out many studies in this vulnerable population is ethically problematic, as well. (This issue will be further addressed in Chapter 5.) Rey, Walter and Hazell (2000) suggest improved education in paediatric psychopharmacology and particularly in alternative treatments, rather than simply tighter control of prescriptions.

2.6 What information is provided to the public about antidepressant use in children?

As data is gradually becoming available, particularly over the past ten years, the NHS in the UK, in accordance with the European Medicines Agency (EMA), and the Food and Drug Administration (FDA) in the US have issued recommendations for antidepressant use in

children. The NHS outlines for public access the three different generations of antidepressant medications, monoamine oxidase inhibitors (MAOIs) and TCAs (first generation), SSRIs (second generation), and serotonin-norepinephrine reuptake inhibitors (SNRIs) (third generation). The safety information provided clearly states that antidepressant use in children under the age of 25 has been correlated with increased suicidality, referring to suicidal thoughts and attempts, in the first few weeks of treatment (NHS, 2010a). Included in the ‘caution’ information, the NHS notes that all three types of antidepressants are not usually recommended for use in children, with the exception of the SSRI fluoxetine (NHS, 2010b). This recommendation follows a statement made in 2006 by the EMEA that it is safe to give children fluoxetine if they are over the age of eight (Lancet, 2006). Further, the NHS recommendations are outlined for clinicians in the guidance presented by the Committee on Safety of Medicines (CSM) and the National Institute for Health and Clinical Excellence (NICE) in 2005, which resulted in the majority of UK clinicians opting to prescribe fluoxetine as the antidepressant of choice. Despite the recommendation for psychotherapy first and prescribing practices described in this guidance as second-line treatment, there is a noticeable discrepancy between the guidance and actual practice (Shearer & Bermingham, 2008; Haw, James & Galton, 2010). The majority of clinicians continue to prescribe antidepressants for most moderately to severely depressed paediatric patients, and want to see revisions in the guidelines to include other SSRIs that may be as safe and beneficial as fluoxetine, such as citalopram and sertraline, which are also commonly prescribed to paediatric patients in the UK (Haw, James & Galton, 2010).

Following a meeting of the Psychopharmacologic Drugs Advisory Committee and the Pediatric Advisory Committee on 13-14 September 2004, the FDA sent a letter to pharmaceutical companies on 15 October 2004 requesting a label change for antidepressants to include a black box warning noting increase risk of suicide in children and adolescents

(FDA, 2010a). A list of drugs requiring this updated box warning, product label, and medication guide was printed on 3 February 2005 (see Appendix C). The FDA produced a revised product label on 2 May 2007 to be inserted into all antidepressant prescription packages. The new label extended the black box warning to include adults under the age of 24, and is the most recent information available (FDA, 2010b). Included on the revised label, the FDA states that fluoxetine (Prozac) is the only FDA-approved treatment for paediatric depression. Further, the use of fluoxetine, sertraline (Zoloft), and fluvoxamine (Luvox) are approved for OCD treatment. All other antidepressants are not FDA-approved for use in children (see Appendix D for full product label; FDA, 2010c).

2.7 What major ethical issues arise in psychiatric care of children and adolescents?

In the US, the American Psychiatric Association published the *Ethics Primer* to provide a useful reference for typical ethical issues that present themselves in psychiatric practice. The chapter regarding child, adolescent, and family treatment calls attention to the following major issues relating to this thesis: informed consent, psychopharmacology, and confidentiality (Arroyo, 2001).

In treating children, ‘consent’ generally falls to the parents until the patient is 18 years of age, with few exceptions, as it refers to the legal permission to treat. The approval of the treatment by the child patient, then, comes in the form of ‘assent,’ which is not to be discounted even though it is not a legal requirement. To consent, and by extension assent, means to agree that the patient has been provided with all the necessary information concerning the proposed treatment, potential risks and benefits, and any alternatives. In fact, inclusion and compliance on the part of the child patient becomes increasingly important as the child gets older, taking more responsibility for their own care and nearing the transition to requiring their own consent. In the US, exceptions to parental consent for minors come in the

form of child emancipation, legal custody issues as related to divorce, foster care, emergency care, and specific procedures as indicated by state legislation.

Particular attention needs to be given to psychopharmacology in the paediatric population. With considerable lack of child-specific data for indications, risks and benefits of psychotropic drugs, psychopharmacological treatment should be taken with caution. The major aspects of concern here are developmental differences, that is physiological differences across the different stages of development, metabolic and toxic vulnerability differences between children and adults, long term effects of a treated versus untreated mental disorder, stigma during an age of identity development, and compliance with parental administration or self-administration of the drugs, especially during adolescence.

Confidentiality is another significant ethical issue in psychiatry which is further complicated when working with children and adolescents. In order to provide the most effective care, the patient must trust the physician, and this trust relies heavily on the physician keeping the patient's consult confidential. As a major issue in adult practices, the physician needs to make it very clear to the patient from the beginning of the consult that confidentiality will be kept except when absolutely necessary to include third parties, such as insurance claims, disclosures that threaten harm to others or the patient him or herself, or indications of child abuse. Where paediatric patients are involved, full confidentiality is hampered by the presence and/or inclusion of parents in the consult and treatment plan. Particularly by adolescence, paediatric patients may become less willing to disclose sensitive information when they know that their parents will be accessing this information; this is less of a dilemma with very young patients, as the young children are typically willing and wanting to disclose details to their parents about what they discuss with the physician.

2.8 In summary, what are the ethical concerns in regards to the development of paediatric diagnosis and care, particularly paediatric depression?

As paediatric care is relatively novel in psychiatry, a number of aspects should receive significant attention when addressing depressed children and adolescents. Firstly, it is important to note the difference in treating a child patient versus an adult. Including the parent in the administration of care to the child raises the issue of what information gets extended to the parent. In general, the parent should be provided with all information required to make appropriate decisions in regards to the child's treatment because the parent must provide consent. However, inclusion of the parent also interferes with doctor-patient confidentiality, and particularly with adolescent patients, this may create difficulty in developing rapport with the patients if they know everything said between the doctor and patient will also be shared with the parent. Further, in terms of child off-label psychotropic use, *informed* consent is complicated by the doctors withholding the extent to which the risks of such treatment are unknown in the paediatric population, as noted by Shearer and Bermingham (2008).

In terms of the diagnosis itself, this systematic label continues to evolve. Neither the DSM nor the ICD are flawless systems to identify depression even in adults. Using one system versus the other may result in individuals receiving a slightly different diagnosis or none at all, specifically in regards to various severities of the disorder. Additionally, considering the limited paediatric clarifications included in the diagnostic description of depression, this raises the question of whether either of these systems provides adequate diagnostic criteria for the paediatric population in particular. Due to the subjective nature of psychiatric diagnosis (to be discussed further in Chapters 3 and 4), systematic classification cannot be perfect, so diagnosis may be approached with a certain degree of scrutiny. As both the DSM and ICD undergo future revisions towards a more dimensional rather than

categorical approach, hopefully the paediatric diagnosis of depression will become increasingly accurate.

Following diagnosis, treatment and availability of information, especially in regard to psychopharmacology, is concerning at present. Despite a lack of long term safety and efficacy data, prescription rates continue to increase significantly. The issue, however, is the vicious cycle referred to by Rey, Walter and Hazell (2000), in that it is ethically problematic both to treat without the availability of safety data but also to conduct extensive paediatric drug research. As more data is presented, trends may change, as reflected in SSRI prescription prevalence following suicide warnings presented over the past decade in both Europe and the US. Until there is a better understanding of what the long term effects of psychotropic treatment are in paediatric application, it should be delivered with caution; however, this is complicated by the observed short term benefits of treatment experienced by many disordered children and long term data presented in adult studies (this topic will be covered in further detail in Chapter 5).

CHAPTER 3

What is disorder and what is normal?: A philosophical perspective

3.1 Why is a diagnosis important?

The previous chapter discussed how diagnoses are made and what it means to be given the diagnosis of paediatric depression. Aside from the mentioned necessity for developing a treatment plan and obtaining insurance coverage, as discussed in Chapter 2, what is meant to be accomplished by psychiatric diagnosis and treatment? According to the Oxford specialist handbook for *Child and Adolescent Psychiatry*, a psychiatric diagnosis serves to ‘collect and organize information collected at assessment’, ‘to guide treatment planning’, and ‘to inform about prognosis’ (Coghill et al., 2009, p. 6). The handbook describes the use of diagnosis and its categorization, matching the discussion of diagnosis in the Hastings Center Special Report on *Troubled Children: Diagnosing, Treating, and Attending to Context* (Parens & Johnston, 2011). Despite the acknowledgment in the DSM-IV that psychiatric disorders are dimensional, describing a continuum of behavioural symptoms, diagnoses are categorical based on the presence of an *arbitrary* number of symptoms (Coghill et al, 2009; Parens & Johnston, 2011). This clinical judgment whether to diagnosis a patient with a specific disorder or not is based on a categorical system that ‘was chosen to maximize the chance that an individual meeting these criteria will be suffering from impairment as a consequence of their [...] symptoms, and that these symptoms and impairments will respond to treatment’ (Coghill et al, 2009, p. 6). Therefore, a diagnosis is generally made in order to identify and treat an impairment that is presumed to hinder everyday life.

However, diagnoses are heavily influenced by social and cultural values and expectations (Singh, 2002; Singh, 2008; Parens & Johnston, 2011). Is it possible that not all

unusual behaviours need to be corrected, even if they lead to a different way of life? Does the resulting ‘abnormal’ lifestyle mean that the quality of life will be damaged? Diagnosis and treatment attempt to improve quality of life, but like diagnosis itself, quality of life is also subjective. The extremities of impairment and quality of life are less subjective; it is clear when individuals have a very good or very poor quality of life, but between the two is more ambiguous, as are the benefits of diagnosing mildly impaired individuals or not, as discussed by Parens and Johnston (2011). Individuals are satisfied with different levels of comfort, both physical and psychological, and often ‘impairment assessments are [...] not always included in diagnostic work-ups’ (Parens & Johnston, 2011, p. S10). Additionally, some discomfort does not always require treatment, but is part of the human experience. So when does discomfort become a disorder?

For adults, it is relatively more clear when discomfort should be classified as a disorder than for children, in part because adults may have a greater ability to process and articulate their experiences, and also because children’s behaviour and mood changes as they continue to develop. Keeping these ideas outlined by Parens and Johnston (2011) in mind, while the boundary between disordered and not may still be slightly blurry in some particular cases, on the whole a disorder can be identified due to an individual’s inability to perform necessary everyday functions. In such a way, those adults who may have ‘abnormal’ tendencies that actually contribute to their occupation or lifestyle are not ‘disordered’ but simply eccentric compared to the ‘average’ person (Groopman, 2000). Rather than interfering with daily functions, certain oddities in adults may facilitate a chosen occupation; for instance, obsessive tendencies may be appropriate in strictly regimented jobs but not in a less structured work environment, whereas unconventionality may be fitting in contemporary art but not in very ordered settings. In an article published in *The New Yorker*, Groopman (2000) describes a group of colleagues discussing their own obsessive compulsive tendencies.

These individuals' obsession with perfection and thoroughness is well suited for their work in a research lab or medical facility where such care to every procedure, safety measure and organization is a valued skill. However, such behaviours may only come to be helpful and appreciated once the individual finds him or herself in an occupation that encourages such behaviours. Life leading to this occupational niche may leave the individual struggling to fit in and make success more difficult in this early environment of primary education and other youth activities, where the individual's differences are not so easily accepted and even frowned upon, as the group goes on to discuss how such behaviours in today's children are often medicalised and treated.

This early struggle is one of the difficulties in identifying disorders in children. A diagnosis is made when the individual cannot normally function; however, at an age when 'normal' functioning is seen only as mainstream abilities, children who are merely 'different' become identified as requiring closer psychological examination and diagnosis. There will be a greater divide between those who are successful in the mainstream environment and those who are not in this population. During childhood and adolescence, individuals are still developing coping mechanisms, so those who are struggling will demonstrate even greater difficulty until they learn how to manage with adversity. Both developing adequate coping skills and finding a more appropriate environment take time and experience, and expecting children to automatically either adjust or seek treatment is too simplistic.

There are cases, however, of genuine paediatric disorders that should not be discounted as simple discomfort regardless of whether they will be overcome naturally with time due to significant impairment experienced in the present. The difficulty lies in determining the severity needed to warrant treatment, which possibly includes medication. Since the baseline for a child's ability to function is largely academic performance and social inclusion, certain individuals may present as disordered based simply on context, while others

would find difficulty anywhere. The former might present as a child who does poorly on schoolwork, shows little interest in participating in activities with other children during and after school, and appears to have few if any friends. The latter might present as a child that often refuses to leave the house and suffers extreme, debilitating anxiety when forced to do so, for example. In the first, albeit an unpleasant experience, the child is struggling but not *unable* to perform necessary daily activities, whereas the second child *cannot* function. It may be beneficial for the first child to receive some non-invasive treatment, such as psychotherapy or enrolling in a more specialized or smaller school program, but the second child may require more intense treatment, such as psychotherapy *and* medication.

Nevertheless, all cases will not be this clear, and any obvious divergence from the norm often raises red flags and causes teachers to suggest and/or parents to seek psychiatric consultation (Parens & Johnston, 2011). Theoretically, physicians will not medicate children who are simply not adjusting to a conventional lifestyle or succeeding in expected ways, in academic or social settings for example, but there is an argument for treating these children presenting with less severe symptoms, as they are experiencing discomfort that interferes with their ability to live a more enjoyable life, which in turn affects their mental health². In a commentary on cognitive enhancement by Greely et al. (2008), the authors note that once the child comes in for a consult, the issue of the role of the physician arises: do physicians only heal patients or do they help their patients live better lives? While there is certainly overlap between these two roles, they are not always the same. The preference may lie with the physicians themselves as they decide which patients should receive treatment, as in the US for instance, or the decision to treat may depend on the policy of the greater health care system, such as the NHS which only treats notable impairment.

² According to the WHO, 'Mental health is defined as a state of well-being in which every individual realizes his or her own potential, can cope with the normal stresses of life, can work productively and fruitfully, and is able to make a contribution to her or his community' (WHO, 2009).

3.2 What is trying to be accomplished through the diagnosis and treatment of paediatric depression?

Treating any psychiatric disorder often only addresses the presentation of symptoms of the disorder, not the cause. This approach reflects a diagnostic system based on behavioural assessment that lacks applicable physiological tests (Singh, 2008; Parens & Johnston, 2011). At present, psychiatric symptoms present as manifestations of causes not readily identifiable or understood, as research indicates that ‘psychopathology results from exceedingly complex and ever-changing interactions among biological and environmental variables’ (Parens & Johnston, 2011, p. S6). There are many biological and genetic markers that may indicate the presence of psychiatric disorder, but such indicators are not *always* as they would suggest. That is to say, the presence of these biological indicators are often linked to a particular psychiatric illness, but sometimes the biological symptoms are present without a psychiatric dysfunction, just as psychiatric disorders may exist without the expected biological symptoms.

Assuming, then, that treatment will not cure a psychiatric illness, a diagnosis serves as an identifier of the *symptoms* that need to be treated. Parens & Johnston (2011, p. S17) indicate that ‘many medications used in pediatric psychiatry [...] reduce the severity of symptoms, or even eliminate them, but they do not “repair” the underlying causes of those symptoms.’ Therefore, diagnosing a child or adolescent patient with depression, for example, indicates that the patient has identifiable and treatable symptoms that may be treated by antidepressants and/or appropriate psychotherapy in order to alleviate the symptoms. Based on this projected treatment plan, these symptoms may be linked to the criteria of ‘depression,’ yielding the ‘paediatric depression’ label for the patient. However, this treatment will not cure the cause of depression, which may be rooted in a complex interaction between biology and environment (Parens & Johnston, 2011).

Referring back to the role of physicians now, if there is no cure, then psychiatrists can only *help* their patients live better lives, not *heal* their patients per se. Consequently, the question for physicians becomes not ‘to help or to heal?’ but ‘who gets help?’ and this raises difficult issues about which treatments actually *help*, particularly in regards to medication, and issues about those ambiguous cases that may or may not be serious disorders. These two issues are closely related, as well. With scarce longitudinal safety and efficacy data for use of most psychotropic drugs in the paediatric population, the long-term effects of taking these prescriptions in childhood is widely unknown, and as such, it is difficult to assess whether the benefits of these drugs for treating psychiatric symptoms will outweigh potential long term risks, particularly as these medications are often prescribed off-label (Shearer & Bermingham, 2008; Singh, 2008; Parens & Johnston, 2011). The decision to medicate the most severe cases is often agreed upon among clinicians as an appropriate method of treatment. In contrast, whether to medicate more mild cases of psychiatric disorders and arguably normal children is an ethical dilemma of overwhelming dispute. In the case of depression, this begs the question of whether or not to give antidepressants to children and adolescents who suffer from mild depression or depressive symptoms. Presumably, these children could likely benefit from medication in the present, but are their experiences and impairments so far out of the normal experience to warrant taking risks that could bring potential unforeseen harm in later years?

3.3 What is normal?

As mentioned above, reason for concern arises when a child does not appear to be ‘normal.’ Western society has an obsession with ‘normal’ that pushes psychiatric care in two directions. The first is the desire to normalize ‘abnormal’ individuals, and the second is the desire to enhance ‘normal’ to improve those who already exhibit healthy mental status

(Singh, 2002; Parens & Johnston, 2011). Before discussing the implications of these directions, ‘normal’ must first be understood. Based on the work of Parens and Johnston (2011) and Singh (2002), and akin to disorder, normal is a subjective social construct and thus is culturally dependent. It may be deduced that in this context, a normal person is an individual who has the common and/or average ability to function in mainstream society and/or a specific societal niche. Normal may be approached as the opposite of disorder and the lack of diagnosis.

Within the paediatric population, normality is measured by such indicators as individuals’ academic abilities, interest in activities, social interactions, general mood, motor skills, and eating and sleeping habits (Carey, 2011). Adult normality may be determined based on similar components, but also has the added context of occupation, ambition, and comprehension of surroundings. While adults have the opportunity to find an appropriate occupation that may complement their way of thinking and functioning to provide a suitable context, children are limited to school and home life; there are only two mainstream measures of normality for children, whereas there are countless contextual and occupational measures of adult normality. For the average child, success falls well within the realm of possibility in the school setting, but for an abnormal child, the same environment is more of an obstacle than a means to success.

3.4 What does it mean to ‘medicalise normal’?

By treating individuals for a medical condition that could otherwise conceivably be ‘normal’, a trend of ‘medicalisation’ of normal has appeared in modern medicine, a classification that is often followed by associated medication treatments. What has been considered within the realm of ‘normal’ life experience in the past is becoming medically classified and treated (Parens & Johnston, 2011). As described by Peter Conrad in a sidebar

of the Hastings Center Special Report (2011), this expansion of medical jurisdiction shifts the causes of any difficulty in life toward internal disorder of the patient rather than the influence of external context and environment. This idea suggests that removing context from psychiatric disorder is excluding a significant factor of mental illness, and becomes a classification of an individual's ability to cope and behavioural tendencies while discounting the experiences that are producing these responses. As described above, normality is relative, and without consideration of environment, any response to life experience could in theory be subject to medicalisation and treatment in order to adjust toward a preferred 'normal' behaviour. Further, if this medicalisation is based solely on the individual, then the treatment will only address the internal symptoms, disregarding the possibility of a needed change in the environment (Shearer & Bermingham, 2008; Conrad, 2011).

Particularly for children, who are still developing, medicalisation requires a closer look. Young brains are in the process of developing, and individual responses to this process may present as noticeable changes in psychological state, which are reflected in mood and behavioural changes that may or may not continue to develop over time into a more recognised 'normal' state. As explained by Parens and Johnston (2011, p. S10):

Determining whether a given child's moods and behaviors are intense enough to be labeled disordered is further complicated by the fact that, as still-developing organisms, their moods and behaviors can be very different from those we see in adults and can vary greatly depending on the age of the child (it may be normal for a four-year-old child to talk with an imaginary friend, but not for a fourteen-year-old or an adult).

As it would seem, in the process of brain development, it is possible that the issue truly is internal, as medicalisation assumes, but classifying this 'abnormal' behaviour and prescribing treatment may not necessarily be the appropriate action. However, just as long term effects of treatment are unknown, perhaps long term effects of no treatment should also be a concern. For disorders such as ADHD, Lahey et al. (2004) show that failure to provide

treatment often results in continued impairment. In regards to depression, Licinio and Wong (2005) note that, while unmonitored antidepressant use puts children at risk of suicide, so too does untreated major depression. Further, Shearer and Bermingham (2008, p.710) suggest that '[social] withdrawal, low self-esteem, substance abuse, self-harm, early pregnancy, academic failure and an increased risk of depressive episodes in the future' may result if depression in children goes untreated. It is difficult to discern if a young patient has the potential to improve with time as he or she develops appropriate coping mechanisms, or if the experienced struggles are too extreme to de-escalate naturally.

Regardless of whether an individual can or cannot naturally overcome psychological distress, though, anyone can benefit from help in times of suffering or difficulty, even 'normal' individuals (Singh, 2008; Parens & Johnston, 2011). In this sense, medicalisation should not be avoided absolutely, just approached with caution. Motivation of medicalisation requires some inspection. Is the aim of treatment to achieve 'normality'? Or taking medicalisation even further, is 'normal' being diagnosed and improved? And if so, what is the issue with improving what is already normal?

3.5 Why medicalise as a means toward achieving normality?

In accordance with the physician's role to help patients live better lives, as noted above, the aims of psychiatry may be split into two subcategories. One is to treat patients in order to approach normality. The intention is to facilitate an easier adjustment to normal expectations, such as academic and social development. Even when an individual is not suffering from severe symptoms, care providers want to provide any amount of support necessary to help the child achieve their greatest potential (Singh & Kelleher, 2010; Parens & Johnston, 2011). Based on this notion, it is ideally assumed that this desire to fulfil potential is a common goal, and that both the parent and particularly the child patient are seeking

success within conventional standards to which he or she is confined. Therefore, in theory, this attempt to be 'normal' does not need to be permanent; presumably, it is only necessary insofar as the child is restrained to the mainstream environment. After this time, the choice to be normal may or may not be as relevant depending on the values of the patient and his or her needs to achieve an acceptable quality of life and success, again subject to the values of the patient. Thus, success within mainstream society in early life often serves as a means to achieve success in the broader spectrum of environments later in life that will follow the generalised early education. This concept is reflected in the discussion by Groopman and colleagues described above; once an individual has completed early education, where abnormal tendencies may hinder more than help, these same tendencies can actually be a valuable attribute for a desired occupation (Groopman, 2000). But before such an occupation can be possible, the individual must be capable of succeeding to some extent within the educational system, which may be allowed through the implementation of medical treatment. Therefore, the idea of correction toward normal in this way is a more accepted aim of psychiatry. It is more closely aligned with the concept of medicine that treats a *problem*. However, given the ambiguous distinction between disordered and normal, Western culture, in particular, is shifting treatments toward enhancement purposes.

3.6 Why medicalise normal individuals for enhancement purposes?

The second and more ethically challenging aim of psychiatry is treating 'normal' individuals. These patients are capable of functioning within the mainstream environment without medical treatment, and do succeed in this context to varying degrees. Medicalising normal in this way is not treating a problem, but rather is *enhancing* present abilities, manipulating consciousness to a certain extent through the use of psychotropic medication, hence labelling this treatment 'neuroenhancement' (Singh, 2008, p. 962; Singh & Kelleher,

2010, p. 4) or ‘cognitive enhancement’ (Greely et al., 2008, p. 702; Farah et al., 2009, p. 541). Enhancement implies that the desired effect is not correcting for deficiencies or atypical behaviours; instead, it is a means of improving normal functioning further than the individual is able to achieve alone. In other words, treatment is not necessary, but it can still advance the patient’s quality of life and ability to function. Generally, these patients are those that may exhibit more minor symptoms of a disorder, which act as barriers to achieving their highest potential, so the patients and/or parents attempt to remove these obstacles by seeking treatment (Singh, 2002; Singh & Kelleher, 2010).

Currently, the predominant practice of cognitive enhancement in the paediatric population is the prescription of neurostimulants, such as Ritalin or Adderall, which are typically used to treat ADHD, but also show enhancement qualities pertaining to focus and attention in non-disordered individuals (Greely et al., 2008; Singh & Kelleher, 2010). Increasing neurostimulant enhancement trends are also found in the adult population, as a means to stay alert in shift work, military service, and within the academic setting to assist in particularly intellectually challenging projects or jobs (Sahakian & Morein-Zamir, 2007; Greely et al., 2008). Proponents of cognitive enhancement prescriptions have equated such treatment to any other form of enhancement. Not unlike exercise, healthy diet, vitamin supplements, sleep, education, tutoring, and other brain-stimulating activities such as reading or music learning, any sort of cognitive enhancement, medicalised or not, will produce changes in the brain (Greely et al., 2008; Singh & Kelleher, 2010). In the commentary by Greely et al. (2008, p. 703), the authors state, ‘Three arguments against the use of cognitive enhancement by the healthy quickly bubble to the surface in most discussions: that it is cheating, that it is unnatural and that it amounts to drug abuse.’ The cheating issue is difficult to address because there are no set rules to indicate what is and is not ‘allowed,’ and if rules did exist, particularly in the academic setting, how would they account for other

enhancements such as caffeine, computer and internet access, hiring of private tutors, etc, which are providing significantly improved learning capabilities and are similarly unnatural (Greely et al., 2008)? Singh and Kelleher (2010, p. 4) suggest that in time ‘the acceptance of drug delivery techniques will normalize, as more and more people choose to take these drugs,’ so this form of enhancement will not stand out as any more unnatural than the other methods mentioned. Further, these drugs are regulated for safety purposes, so if such regulations are followed abuse should not be a worry (Greely et al., 2008). The motivation to medicate in this context, then, is not unlike any other measures taken to aid intellectual development and academic achievement.

3.7 What additional ethical considerations arise when medicating normal children?

Based on the arguments above, medicating normal children, that is cognitive enhancement, is not entirely different than other aids in the benefits that it could provide individuals. On the other hand, there are other serious risks and ethical concerns that are distinct about medicating otherwise normal children and adolescents. Greely et al. (2008) highlight three major considerations, safety, freedom, and fairness, which mirror similar concerns raised in regards to neuroenhancement of adults, as well (Sahakian & Morein-Zamir, 2007). For children, whose brains are still in the process of developing, giving them psychotropic drugs which will significantly alter brain chemistry can cause unforeseen effects both at present and later in life (Singh & Kelleher, 2010). Furthermore, the effects that psychotropic medication has on disordered versus normal brain development may be significantly different, as well, due in part to different dosing and to variation in neurophysiology. In their discussion on neuroenhancement, Singh and Kelleher (2010) identify this as an issue in regard to methylphenidate enhancement noting:

There are likely to be different implications of treatment use of methylphenidate and enhancement use of methylphenidate for

the developing brain. This is because dosing practices for these two different uses of the drug will likely differ, with enhancement doses focused on short-term events and treatment emphasizing ongoing use over long periods; in addition, pre-existing structural and functional variations in the brains of those diagnosed with a clinical disorder as compared to undiagnosed persons may mediate the impact of methylphenidate on the developing human brain. (p. 6)

The long term data for use of these medications in children is still fairly limited even in severely disordered children. While such treatments may possibly be safe to use in children, both prescribed at a young age and/or over a long period of time, until there is significantly more data to prove such safety, the question becomes is it worth unknown risks in children that are essentially normal (Shearer & Bermingham, 2008)? (Physiological concerns will be addressed further in Chapter 5.)

Freedom, the second concern raised by Greely et al. (2008), needs to be considered, particularly in regard to coercion. The authors suggest that if cognitive enhancement becomes the norm, then individuals may feel that they have to seek medication to compete with their peers. This idea implies that even if individuals theoretically have the choice to either medicate or not, they will be pressured to medicate in order to be on the same level as their medicated classmates. Moreover, children are not free to make their own medical decisions, so they are left to their parents' decisions. Parents may be pressured by the general desire to see their children succeed, but also to fulfil the cultural construct of a 'good parent.' In the words of Singh and Kelleher (2010, p. 9), 'cultural notions of "good mothering" place a burden on mothers in consumer-driven Western societies to access and exploit all available resources to ensure a young person's success.' Such resources could include cognitive enhancing drugs, e.g. neurostimulant, and if these enhancement practices do become normal practice then withholding psychotropic resources will be viewed as restrictive (Singh & Kelleher, 2010).

With competition as a driving force to medicate, fairness becomes an issue. Greely et al. (2008) explain that if the enhancement is temporary, boosted performance is an unfair advantage of taking medication, whereas long term enhancement could be more comparable to other non-medical resources used for enhancement to improve learning. The authors equate the use of short-term enhancement to allowing some students to use a calculator on a maths exam while others cannot; in such a case, comparing those with enhancement to those without is not a fair measure. Based on this argument, if enhancement was a more long-term aid, an individual's performance would better reflect actual competency as the medication would improve overall learning abilities, not simply the direct effects of a drug that would allow one to learn a specific task or piece of information. However, most research suggests that stimulants, at least, show short-term, not long-term, improvements (Singh & Kelleher, 2010; Parens & Johnston, 2011). Therefore, it would seem unfair to allow the use of neurostimulants unless everyone had access to this resource. At present in the U.S., 'prescription rates vary by race/ethnicity, religion, gender, and socioeconomic status' (Singh & Kelleher, 2010, p. 9), trends which appear indicative of different social influences across these varying demographics. Since the choice to medicate could interfere with sociocultural values, even fair access could also be tied back to coercive influences on freedom as discussed above. As a result, depending on its accessibility, costly medication may further splinter socioeconomic classes, yielding an increasingly advantaged wealthy class (Greely et al., 2008; Farah et al., 2009). Though, if distribution did become more even, then issues of the upper limits of human capacity and threshold for disorder and/or disability would alter significantly, skewing concepts of normality even further (Singh & Kelleher, 2010). Therefore, being human would no longer be enough; one must medicate to be successful in the enhanced society.

Another ethical issue suggested by Farah et al. (2009, p. 542) is ‘the effect of cognitive enhancement on what could be called “cognitive style.”’ This concept is referring to the *way* people think. Enhancement has been addressed as a means of improving patients’ ability to think clearly, but does treatment also affect what an individual thinks in addition to how well he or she processes thought? This questions whether a medicated brain actually changes the thoughts themselves, as indicated by creativity for instance, which is defined as ‘the process of accessing seemingly irrelevant or unrelated information in ways that serve a purpose or solve a problem’ (Farah et al., 2009, p. 542). But why should it matter if medication changes thought? The authors suggest that this change would create negative societal effects, resulting in ‘less creativity in our workforce and in our leaders’ (Farah et al., 2009, p. 542). Though what do they mean by this, and is this assumption too pessimistic? Based on the definition given above, creativity would seem an essential element of progress, so if modern industry and leadership became lacking in creativity, as Farah et al. suggest, then novel solutions to current and forthcoming issues may become less productive, stunting improvements in business, politics, society, and culture. However, the results of this study indicate that there is ‘no evidence of a general impairment’ (Farah et al., 2009, p. 546), and even an improvement was shown in less creative individuals. There was only a concern raised regarding the lowered convergent creativity, which is making associations between elements of provided information, in highly creative individuals, suggesting that similar to the effects on cognitive abilities, neuroenhancement may actually impair high ability individuals. Given that overall, there is no impairment of creativity, and further, a possibility of improved creativity in previously less creative individuals, the research would actually seem to suggest a more collective positive societal effect if enhancement becomes normal practice, despite the negative effect on the most creative individuals.

3.8 How might cognitive enhancement relate to antidepressant use?

In the adult population, there has been a notable trend over the past couple decades of antidepressant enhancement use, especially with Prozac (fluoxetine). Paralleling, and perhaps fuelling, medicalisation, which has increased the number of diagnosable disorders and associated drug treatments, extended indications of Prozac for enhancement purposes allows a new way to describe, categorise, and evaluate individuals and life experience (Elliott, 2004). Parens (2004) comments that those people who are able to help individuals struggling to achieve a ‘normal’ life, disordered or not, should provide such relief when possible, even if medicalisation is a cultural problem, because ‘people who suffer want and deserve relief’ (p. 26). Prozac, and presumably other similar drugs, allow suffering individuals to regain a sense of autonomy and control over their life, who they are, and how they interact with the world, a transformation described by Peter Kramer in his book *Listening to Prozac* (cited in: Valenstein, 1998; Degrazia, 2000; Parens, 2004).

Reflecting Kramer’s anecdotal explanations of Prozac enhancement, Degrazia (2000) explores the ethical issues associated with using antidepressants for enhancement through the case of a woman who is requesting a prescription of Prozac in order to improve herself and overcome personal difficulties. While there is no diagnosable disorder, the change is sought in hopes of increasing confidence and decisiveness and decreasing obsessions and the impact of perceived negative social interactions. The discussion following the description of this case outlines similar issues to those raised above with neurostimulant enhancement in children: fairness, freedom, safety, that it is unnatural, that it changes who we are, and the implications of medicalisation. In large part in this context, fairness refers to access to enhancement drugs; consequently, if enhancement became the norm, it would most likely be a luxury of wealth and act to further widen the socioeconomic gap. Also, as enhancement normalises, the freedom to medicate would be controlled by the pressure to compete with the

rest of the population; in a society where everyone is medicated, medication would not promote advantage over others, but instead would level the competition, whereas the choice not to medicate would be a disadvantage. While the safety of antidepressants is thoroughly tested in depressed adults, the risks of medication in otherwise normal adults are widely unknown, particularly with regard to appropriate dosages, the amount of physician monitoring required and long-term effects. However, antidepressant enhancement would not be any more unnatural than other means of psychological and/or biological neural change, for instance psychotherapy, and merely reflects an individual's values with respect to the method opted to evoke such an adjustment.

Therefore, the desired transformation itself should be the ethical concern, not the means of attaining it, which is the issue of changing *oneself*. This idea of altering and manipulating personality raises questions of identity and authenticity mirroring the cognitive style argument by Farah et al. (2009). While Elliott claims that such changes to a person would deem the result inauthentic, something other than who that person truly is, Degrazia says the opposite, calling the process 'self-creation' (Degrazia, 2000, p. 35). He suggests that the transformation accomplished through antidepressant use creates another version of oneself, not a *different* person, and as long as this 'new' person fits one's conception of self, what is valued by the individual, and how the individual identifies him or herself, then it is authentic (the concept of identity will be discussed further in Chapter 4). Furthermore, it is within human capacity to change, either by choice or inadvertently over time, but such capacity is also limited by genetic, developmental, and environmental factors, as well as uncontrollable consequences of human choice; so while individuals may choose to take antidepressants to manipulate their personality or identifying qualities, such control is not unbounded.

The remaining issue with regard to adult antidepressant enhancement is the rise of medicalisation. As discussed above, medicalisation removes the emphasis on context and tends to diagnose, and often treat, any struggles within formerly ‘normal’ life experience. Opponents to enhancement argue that medicalisation and treatment diminish the sense of autonomy in individuals. This line of reasoning is countered by the assertion that the choice to pursue enhancement methods for self-improvement is an act of agency itself, as well as the original reasons for seeking treatment being perceived as controlling and hindering one’s agency, hence the desire to change. At the individual level, then, the increased use of diagnosis and treatment may show positive implications; however, at the societal level, this trend may be more troubling due to the cultural values it promotes (Degrazia, 2000) (the cultural implications of which will be discussed further in Chapter 6).

3.9 Could antidepressant enhancement extend to the paediatric population?

The ethical issues raised regarding the trend of cognitive enhancement in young people have generally referred to the use of neurostimulants, but antidepressants have also shown improvements in normal individuals, as indicated by the discussion of adult enhancement above. However, at present, there are no published trials on antidepressant enhancement use in children or adolescents (Singh & Kelleher, 2010). Although, given what is known about the enhancing qualities of antidepressants, could the future of paediatric antidepressant use include enhancement purposes as well? What would the benefits be for normal people if not treating a disorder? Typically, antidepressants do not make users happy, *per se*, but balance overwhelming negative mood, stabilizing the individuals’ personality. Applying this to normal individuals, such treatment might be expected to stabilize anyone’s personality and provide more clear thought processing, reducing anxiety and stress and increasing confidence. Unlike neurostimulants, which help to focus thoughts, antidepressant

enhancement is used for performing in high-anxiety activities, such as ‘public speaking, sports performance, and musical performances’ (Singh & Kelleher, 2010, p. 4). This suggests that antidepressants would be used to dissipate restrictive thoughts and/or moods that could otherwise impede performance, allowing performers to achieve their full potential in more stressful conditions.

Although, in view of the negative media attention given to antidepressant use in children after the updated black box labelling and suicide warnings, as discussed in Chapter 2, using antidepressants in this population for enhancement may not occur in the immediate future. However, considering that antidepressants are the second most common psychiatric prescription for children and adolescents, only after neurostimulants (Zito et al., 2000; Rushton & Whitmire, 2001), it is not unrealistic to consider the possibility of an emerging enhancement trend. Once more safety and efficacy data is presented for antidepressant treatment in disordered paediatric patients, the next turn will go toward the same treatment in normal children and adolescents. If these future studies on antidepressant enhancement in the young population see any possibility of positive results, particularly with the influence of pharmaceutical marketing, a trend mirroring that of neurostimulant enhancement could certainly be expected.

With this possibility in mind, in addition to the ethical issues presented above concerning paediatric neuroenhancement, the shaping of personality by antidepressant enhancement raises further questions. Similar to the ‘cognitive style’ argument and its extension to adult antidepressant enhancement, this concept requires examination regarding whether it is acceptable to manipulate the way children and adolescents think, as the decision to medicate is not solely theirs to make. Personality, like creativity, reflects who individuals are fundamentally, the authentic self and identity. Medicalising normal personalities is diagnosing and treating what it is that makes people uniquely human; would this practice

discount human experience? How people think and act is largely a result of experience in combination with biology. Psychotropic medication alters biology, shifting this combination of influences towards biological causes. By allowing the use of antidepressants in this way without full attention to the desires and needs valued by the paediatric patient, it would seem unethical to change how the patient will feel as a person. However, is this giving too much credit to antidepressants' ability to alter the mind? This presumption may in itself be discounting experience and psychology, which may not be lessened by manipulating biology, but rather altered itself. These issues regarding the effects of medication on identity and experience will be addressed in Chapter 4.

3.10 In summary, what are the ethical concerns involving antidepressant use with regard to medicalisation and enhancement of normal paediatric patients?

The subjective nature and arbitrary classification of diagnosis typically allow identification of those individuals who possess treatable symptoms of a disorder. Level of impairment experienced by the individual, and thus the degree of need for treatment, is determined by his or her ability to function in his or her environment, which is generally limited to home and school during childhood and adolescence. This implies a certain dependence on context in determining treatment; not only must the patients themselves be treated, but their environment must also be considered. In the case of depression, a treatment plan involving psychotherapy and medication may address the patient's symptoms, but additional life stress in his or her environment should also be taken into account.

However, as medicalisation of normal sweeps through Western culture, less emphasis is placed on a child's context and more on the ability to clinically improve a struggling individual. With the existence of medications that may benefit not only disordered patients but also normal individuals, providing such treatments even in the absence of clinical

impairments is becoming more common practice in order to allow individuals to succeed to their fullest potential. Currently, the limited efficacy and safety data for psychotropic use in the paediatric population provide a very unclear balance between the benefits and risks of off-label prescriptions for disordered, let alone normal, children and adolescents. This challenges a physician's certainty that he or she is helping a patient who may arguably be unimpaired without treatment. Hence, antidepressants are rarely used for enhancement purposes in the paediatric population. Nonetheless, given that neurostimulant enhancement is common in children and adolescents, and SSRI enhancement has been practiced in adults for decades, it is not unreasonable to predict that this practice may extend to antidepressant enhancement in children in the future.

CHAPTER 4

What does paediatric depression mean in terms of psychological development?: A psychological perspective

4.1 To what extent can we apply adult diagnoses to the paediatric population?

Chapter 1 discusses how the adult diagnosis is adjusted to fit the child presentation of psychiatric disorders, but is this a frivolous attempt to apply an adult-centric concept of diagnosis? Rather, would it be more effective to create entirely separate diagnoses to apply to children? Considering the uniqueness of the paediatric presentation, classifying a distinct diagnosis may be more effective at identifying affected individuals as the symptoms will be more population-specific. Often affected children and adolescents do develop adult disorders, but treatment of paediatric versus adult symptoms will be different, as additional consideration should be given to children as developing humans, both psychologically and biologically. Biederman et al. (2003) calls attention to this issue of diagnosis in regard to paediatric bipolar disorder, noting factors which make diagnosing in this population particularly difficult. By comparing the atypical features of the paediatric presentation to that of adults, the former seems to take its own form, which often develops into the more familiar presentation, that of adults, only later in life, with adolescents' symptoms most closely resembling the paediatric presentation. In addition to atypical presentation, paediatric diagnosis is difficult due to high levels of comorbidity, overlap with other disorders; Biederman et al. (2003) call specific attention to the overlap of paediatric bipolar disorder with ADHD and conduct disorder (CD). Another important factor identified is familial aggregation, the tendency for disorders such as paediatric bipolar disorder to have high prevalence within affected families. While the familial aggregation of bipolar disorder is widely accepted, similar trends are not an uncommon feature of many other psychiatric

disorders, but often genetic and environmental influences cannot be disentangled. The Beiderman et al. (2003) study goes on to evaluate common treatments. Through studies such as this study of bipolar disorder, other paediatric disorders, such as depression, may be more easily identified and appropriately treated.

While no one individual study has gathered information about paediatric depression by aligning identifying features followed by an evaluation of available treatments in the way that Biederman et al. (2003) have done for bipolar disorder, Rao and Chen (2009) have elaborated on the identification and understanding of paediatric depression through a developmental psychopathology study of the epidemiology, clinical presentation, prognosis, and risk factors. Developmental psychopathology is a new method of researching psychopathology that considers the influence of developmental processes as reflected in differences in a disorder over a lifetime. By integrating studies of depression across different age groups, Rao and Chen (2009) highlight that depression appears to be increasingly common at younger ages, though such trends are difficult to interpret due to ‘increased clinical awareness of early-onset depression and changing diagnostic criteria’ (p. 3). However, given that rates of depression have notably levelled out by early adulthood, it can be inferred that childhood depression may not just be a more recent problem, simply more recognised. Further, it is noted that children who experience depression show psychosocial disturbances, not developing in the same way as their unaffected peers, but whether the depression causes this disturbance or vice versa is unknown, which is further complicated by the effects of comorbid psychiatric disorders, low socioeconomic status, and other life stressors (Rao & Chen, 2009; Ngui et al., 2011).

Rao and Chen (2009) go on to describe the clinical presentation, noting the differences in children as compared to adults, specifically in regard to symptoms listed in the DSM IV-TR criteria (as outlined in Table 4.1 below). Another developmental trend is the

observed gender difference in prevalence rates, depression becoming increasingly more common in girls than boys with increasing age. Also associated with gender and age is the prevalence of comorbidity of depression with other psychiatric disorders. While there is a shifting of symptoms from the paediatric presentation to that seen in adults, recurrence rates following a major depressive episode in childhood mirrors rates found in adults, and though not predictive of developing depression in adulthood, often leaves individuals at risk to adult depression. Risk factors associated specifically with paediatric depression include the vulnerability imposed by the plasticity of development itself throughout childhood and adolescence (physical, cognitive, social, interpersonal), familial transmission (both genetic and environmental influences), neurobiological abnormalities (to be discussed in Chapter 5), difficult temperament, negative cognition, negative interpersonal relationships, stress and vulnerability to such stress (Rao & Chen, 2009).

Table 4.1: Key symptoms of depression compared by age group. Combining results by Rao and Chen (2009) and Ginicola (2007); it is important to note that while adolescents are shown here with adults, they present symptoms on a continuum between the two groups, but tend toward internalising their disorder.

Child	Adolescent/Adult
Irritability	Depressed mood
Behaviour problems	Melancholic symptoms
Aggressive behaviour	Feelings of guilt
Changes in psychomotor patterns	Worthlessness and hopelessness
Somatic complaints	Psychotic symptoms
Auditory hallucinations	Delusions
Self-injuring behaviour	Suicidal thoughts/attempts with high lethality
Comorbid mixed disorder	Comorbid internalising disorder
	Hypersomnia

Investigating the shift from child to adult psychiatric presentation through the developmental approach, research by Ginicola (2007) looks specifically at the shifting of depressive symptoms from early childhood through adolescence. This study correlates symptoms to ‘mental age’ (Ginicola, 2007, p. 2), a combination of chronological age and IQ to determine the developmental level of subjects in order to account for differences in the rate

of psychological development between individuals. The correlation that was found reflected younger children demonstrating more external symptoms which gradually changed toward more internal symptoms later in development (as reflected by the symptoms outlined in Table 4.1 above). Ginicola (2007) concludes that these significant differences in presentation must be taken into account when diagnosing and treating paediatric depression.

4.2 Are these children really experiencing a psychiatric disorder or are they just learning to cope with growing up?

Since affected children often show such inconsistencies with adult diagnoses, it may appear that these individuals are not disordered at all. This is due in part to their stage of life. Children and adolescents have limited life experience, so how can they truly experience a psychiatric disorder if their mind is still in the process of developing? It is possible that some children have not developed adequate or appropriate coping mechanisms to deal with stress, defined as ‘environmental conditions that threaten to harm the biological or psychological well-being’ (Rao & Chen, 2009, p. 12). For some children, this stress may be the common stressors, such as school transitions, conflict exposure or loss (friends moving away, pets dying); for others the stress may be more pathological, for instance trauma, abuse, or physical illness (experienced either by the individual or a family member) (Coghill et al., 2009; Rao & Chen, 2009). Whatever the cause of psychological discomfort may be, young individuals have rarely had the opportunity to develop their own means of coping with life that is acquired through experience, and therefore, have not yet learned to deal with negative or stressful events appropriately. This inability to cope leaves the child vulnerable either to the negative impact of stress and/or the development of maladaptive responses to stress, hence stress acting as a risk factor of depression, as mentioned by Rao and Chen (2009). What level of psychological discomfort, as expressed through depressive symptoms for instance, is

necessary to warrant diagnosis and treatment, then? Further, abnormal coping strategies may easily be identified as a psychiatric diagnosis and treated accordingly, but is that a fair assessment of the situation in context? Treatment in this case could certainly be beneficial, at least in the short term, but it also provides the child with an alternate coping mechanism that may interfere with the ability for an individual to develop his or her own coping strategies. When faced with a problem, such an identified child will often be brought to a physician by a parent not knowing an alternative to alleviate the child's distress, and it may be suspected that over time the patient may independently turn to psychiatric treatment because he or she is unaware of any other effective strategy (Shearer & Bermingham, 2008). Every child develops at a different rate, some children simply need more time to learn appropriate coping skills, which is why Ginicola (2007, p. 2) takes into account both chronological age and IQ to calculate a more applicable 'mental age' when studying psychological development and symptoms in depressed children. That being said, there is a difference between children and adolescents who will develop coping mechanisms naturally with time and those who are, in fact, disordered and require treatment. Again, this addresses the difference between 'normal' and disordered. Similar to disordered adults, disordered children often lack appropriate coping mechanisms, which then tend to generate additional stress (Rudolph & Klein, 2010); thus, to counter their maladaptive coping skills, these children require treatment. There is certainly validity to paediatric experience of psychiatric disorders; however, it must be acknowledged that such experiences are very unique to this population, i.e. not to be confused with the adult experience of a disorder. Again, through studies such as that conducted by Biederman et al. (2003) and Rao and Chen (2009), identification of those individuals that need treatment will be clearer, and more accurate diagnoses may be applied.

4.3 What is identity and concept of self? How do the diagnosis and/or disorder affect one's development of identity and concept of self?

At a crucial age for identity development and self-understanding, deviations from 'normal' development, however subtle, have the potential to impact a child's concept of self substantially. Identity, self-understanding, and concept of self will be used interchangeably here, as found in psychiatric literature, referring to an individuals' awareness of what they need and want, how they perceive the environment's impact on themselves, and how they perceive their impact on their environment. Coghill et al. (2009) define self-concept as:

An individual's awareness and the set of beliefs and attitudes that a person holds about themselves [...] Many aspects of self-concept are unique to humans and higher-order primates as these are the only species that have the capacity to see themselves as both *subject* (e.g. 'I', the person looking in the mirror) and *object* (e.g. 'me', the person being looked at). (p. 22)

The description goes on to divide self-concept into three major components: self-image (description of self, both objective and subjective), the ideal self (who an individual wishes to be), and self-esteem (perceived self-worth, often dependent on the comparison of the former two components). Further, it is noted that the development of self-concept is a fluid process over a lifetime, beginning with an infant's recognition of his or her own physical self, followed by an older child/adolescent developing a psychological understanding of self (Coghill et al., 2009).

As indicated by the risk factors of paediatric depression outlined above by Rao and Chen (2009), adolescence is a time of significant psychological vulnerability, and it may be inferred that this vulnerability refers in part to the plasticity of a developing identity. Through their research of depressive personality in children, Rudolph and Klein (2009, p. 6) note, 'Because personality traits are still under construction during childhood, experiencing significant psychopathology may leave a developmental "scar."' This concept implies that the experience of a psychiatric disorder during childhood is going to have a significant impact

on a child's developing understanding of self. Rudolph and Klein (2009) believe this to be a negative 'scarring' influence in regards to depressive symptoms, as they later state, 'Experiencing significant depressive symptoms and associated impairment early in life may undermine youths' sense of self and disrupt their emotional development, leaving youth feeling ineffective and pessimistic and creating lingering emotion dysregulation' (p. 21). The implication is that negative self-concept developed early in life as a result of experiencing paediatric depression will persist into adulthood, whether in the form of adult depression or depressive personality; the disorder becomes incorporated into the individual's identity and to some degree leaves a lasting effect.

Floersch et al. (2009) studied the integration of experiencing a disorder and treatment into adolescents' developing concept of self. They conducted interviews with adolescent patients being treated with psychotropic medication, investigating how their experience of their illness and treatment shapes the subjects' view of themselves, identity, ability to cope, and relation to others, providing valuable qualitative information about psychological effects of psychiatric treatment in this population. Adolescent subject responses in the interviews in this study were coded to link quotations to emerging themes, resulting in the following:

- (i) emotion—references to emotional problems; (ii) diagnosis/disorder/symptom—reference to psychiatric illness, disease, or diagnosis; (iii) self—reference to some aspect of the self as the problem; (iv) cognition/thought—reference to cognitive problems; (v) intersubjective—reference to relationship problems; (vi) body—reference to physical problems, and; (vii) behavior/action—reference to behavioral or school problems. (Floersch et al., 2009, p. 5)

Often children, particularly adolescents who are beginning to gain self-awareness, can recognise their own disorder to some extent. The work by Floersch et al. (2009) implies that sometimes an affected child may realize that, to varying degrees, he or she interprets the environment much differently than his or her peers, feels emotions or processes thought in unusual ways. For example, a depressed child may notice that he or she does not enjoy

activities like other ‘normal’ children appear to. More often, however, teachers and peers may notice differences in the individual’s behaviours and ways of interacting with others, resulting in that child experiencing a perceived rejection by others more than an awareness of psychiatric experience, as pointed out by Rao & Chen (2009). Such factors may have greater influence on a very malleable developing identity, compared to a presumably more secure adult identity, perhaps causing a sense of self-identified isolation or eliciting negative interpersonal relationships, which then exacerbate the negative experience of a disorder.

As mentioned in the emerging themes listed above, many disordered adolescents make reference to their disorder and/or diagnosis. Providing a label that indicates abnormality may have additional influence on identity development because it puts an identifiable name to the behavioural experience. As demonstrated by the research of Floersch et al. (2009), this label can then be incorporated into children’s developing concept of self as a significant part of who they are and how they view themselves. Some individuals externalize their diagnosis as an experience that they are treating; others recognize the disorder as a part of who they are internally. Floersch et al. (2009, p. 5) point out the difference between the children believing that the diagnosis is *who they are*, ‘I am ADD,’ compared to something that affects them: ‘I have depression.’ Based on qualitative studies such as this, it may be suggested that the internalization of diagnosis into identity may be helpful for some individuals while detrimental for others. By integrating a psychiatric diagnosis into who they are, certain children and adolescents may find such a facet of their identity better explains who they are, allowing both them and others to have a fuller understanding of themselves, a positive result of assigning a label to their atypical experiences. Similarly, even for those patients who externalize the diagnosis, an available label can provide validation for their experiences as well as feelings of community; they are not alone and enough other people have similar feelings that their symptoms have been

grouped into an identifying label. On the other hand, a negative effect of internalizing diagnosis may be development of helplessness and isolation produced by the stigma surrounding psychiatric illness. With a label to identify them as abnormal, a diagnosis defines them as different from their peers, incorporating negative connotation and stigmatism into who they are, not simply possessing individuality but a noted deficit. Further, if these diagnosed children view their disorder as a part of themselves, they may perceive attempts to improve their mental illness as futile or creating a self-conflict as they are encouraged to change *who they are*, not just how they act. Thus, treatment will have additional impact on understanding of self, which will be addressed below.

Floersch et al. (2009) suggest another prevalent issue that follows identifying with a disorder and/or diagnosis: for a population so commonly diagnosed with comorbid disorders, the question becomes which diagnosis does an individual identify with? Based on the understanding of incorporating diagnosis into identity, as described above, the diagnosis with which a patient identifies most strongly should be one that deserves the greatest attention in terms of treatment because presumably it is the most influential with regard to the patient's ability to interact and function within his or her environment. However, with such strong association between the patient's concept of self and a particular diagnosis, such treatment should also be approached with additional consideration, as it is more personal to the patient than other disorders being experienced simultaneously. That is to say, treatment of a diagnosis that is a greater part of a patient's identity will be expected to hold greater meaning to the patient and make a more significant impact on the patient's understanding of him or herself and interaction with the environment, whereas treatment of the less meaningful diagnosis will be expected to be less influential in affecting a patient's self-concept. As mentioned above, Biederman et al. (2003) note the difficulty of making a diagnosis due to high comorbidity rates; would it be useful in paediatric psychiatry to create more specific

diagnoses that incorporate what currently exist as distinct but commonly comorbid disorders? For example, rather than diagnosing a child with depression *and* conduct disorder, the new diagnosis would be *one* diagnosis that would be a combination of the two, such as ‘depression with conduct disorder’. Perhaps this would disentangle the complexity of incorporating multiple diagnostic labels into a child’s developing identity, or would it complicate the already complex integration of diagnosis into identity formation?

4.4 How does the experience of psychiatric treatment affect a young patient’s development of identity?

Just as special attention is given to the child/adolescent experience with medical caregivers, such attention must also be applied to the patients’ experience with the treatment itself and how it affects their understanding of themselves. While in the process of developing their identity, children and adolescents integrate their personal experiences along with others’ perceptions of themselves into their concept of self (Rao & Chen, 2009). In other words, they form their identity by combining how they interact with the world and how the world seems to react to them. In regard to adolescent psychiatry with relation to identity formation, in their investigation of effective psychopharmacology and motivational interviewing (described below) Dilallo and Weiss (2009, p. 110) comment, ‘Therefore, any information communicated to an adolescent about diagnosis or treatment options will be incorporated into his or her process of self-definition.’ Psychiatric treatment at this age will take a greater effect in shaping the patient’s identity than experiencing such treatment later in life when an identity has already had time to stabilize. Therefore, it is important to understand how paediatric patients view their own treatment, how such treatment influences their view of themselves, and how much participation and responsibility they take in their treatment plan, for example incorporation in the consultation (as discussed in Chapter 2) and

willingness and motivation to follow prescriptions, both of which may be directly proportional to patient age.

In the context of children taking neurostimulants for ADHD treatment, Singh (2008) and Singh and Kelleher (2010) discuss the impact on child identity. Singh (2008) notes the limited empirical data available despite the amount of debate on the subject. Many people call attention to the potential harms of medication to individual autonomy and identity, stigma associated with medication, and interference with the natural experiencing of childhood as a protected state of innocence; however what the evidence actually shows is children expressing positive effects of treatment on their sense of authenticity, at least prior to adolescence. Singh and Kelleher (2010, p. 8) highlight this issue noting ‘strong concerns about potential threats to a young person’s identity, agency, and responsibility because of the alterations in motivation, attention, interaction with others, and performance for those young people taking them’. This argument is referring to the child’s development of ‘moral self-understanding’ (Singh & Kelleher, 2010, p. 8), which may be taken to mean one’s feeling of control over who they are (authenticity) and their behaviour and interactions toward others (responsibility). Again, these ethical arguments are countered by the evidence that younger children, at least, attribute more positive impact of medication treatments on their sense of control over their actions (agency), thus having greater ability to create a desirable outcome for themselves. In terms of the negative attributes of labelling and stigma of psychiatric treatment, Singh and Kelleher (2010) note that bullying and negative interpersonal relations actually tend to improve for medicated individuals as compared to the negative interactions experienced as a result of ADHD-type behaviours prior to medication. While these positive effects on personal identity should be considered, an observed complication in understanding a notion of responsibility arises, as well. Some children express attribution of good behaviour to their medication and/or blame bad behaviour on a lack of medication; rather

than taking personal responsibility for their actions, children taking stimulants use their medication as the agent of their behaviour. As suggested by Singh and Kelleher (2010), the extent to which children actually believe their medication explains their behaviour or if they are simply using medication as an excuse requires further study. Additionally, both Singh (2008) and Singh and Kelleher (2010) omit any specific comment on medication impact on adolescent identity development, what does this older paediatric population experience, or is the evidence even more lacking than that for younger children on this subject?

Relating the above discussion of neurostimulant treatment to the use of medication for treatment of paediatric depression, parallel arguments may be presented. Those opposing medication may argue that medication will interfere with authentic childhood experience, which is the 'nurture-neuroethics argument' (Singh, 2008, p. 962). By giving children antidepressants, these children will experience an unnatural childhood; however, this outlook risks discounting the harm of a child experiencing a significantly depressive childhood, which also greatly impacts the 'ideal state of innocence and freedom' (Singh, 2008, p. 962) that is the experience such proponents of this argument wish to protect. Supporters of medicating children may counter this unnatural experience by pointing out the positive effects of medication. As discussed above, children experiencing depression tend to have negative interpersonal experiences; thus, medication may improve relationships in a similar fashion to the way neurostimulants have (as described above). Furthermore, medicated children may be able to take greater control of their actions and positively affect the outcome of their behaviours, where depressive behaviour may have seemed to control them prior to psychotropic treatment. Then again, developing a sense of responsibility will likewise be complicated. If the argument presented by Singh and Kelleher (2010) is applied to antidepressant treatment, children may use medication as an explanation of positive and negative behaviour and temperament rather than placing themselves as agents of control; any

good moods may be attributed to medication, while poor moods and disinterest may be excused by lack of medication. Depressed children who are medicated, then, might not only discount personal agency, but also the impact of personal experience.

4.5 How does expectation for their treatment relate to child and adolescent experience of and receptiveness to treatment?

Receptiveness to treatment can be notably affected by patient expectations and influence by others. The study by Floersch et al. (2009) explores the gap between expectation and experienced effects of treatment and medication in the paediatric population. As a qualitative study, the aims addressed the views held by adolescents treated with psychotropic medication in regard to their illness (as discussed above), their understanding of how their medication works, and their role in their own treatment. Since expectations for psychiatric treatment are much less distinct, the difference between expected and experienced effects shows significant variability. The authors discuss the expectation to experienced effects of psychotropic medication compared to that of medication for a more discrete condition such as a headache. When a patient takes medicine to treat a headache, the expectation is that the headache symptoms will be alleviated, and generally the actual effect of treatment is an experience very similar to that expectation. In contrast, the ambiguity of expectation for psychotropic treatment makes it difficult to pinpoint a reference to compare to the experienced effect. As such, expectations are more skewed due to the limited knowledge of efficacy and long term effects.

In terms of experienced effects, the data reported indicates ‘a belief that medication produced behavioral change’ and ‘parents and others influenced their experience and understanding of illness and medication’ (Floersch et al., 2009, p. 5). Changes in behaviour led many adolescent subjects to note particular improvements in interpersonal relationships

and emotional stability. As for expectations subjects had for their treatments, the following sentiments were communicated: ‘provide a cure; control their anger [...] not stop working [...] relieve family stress’ (Floersch et al., 2009, p. 5). Many expectations revolved around the influence of other people as well as the impact on others in their environment. For example, the adolescents relied more on the knowledge of their medication imparted to them by their parents, doctors, and media to form their treatment expectations and even to understand their own experiences and feelings. This weighted reliance on others in order to understand themselves suggests a level of plasticity in adolescent identity formation that will fade over time. Presumably, by adulthood, while the influence of others on their self-understanding may not disappear entirely, it will diminish as they come to know themselves better. Additionally, adolescents noted an expected influence their treatment would have on others as a motivation for following prescribed treatment plans, taking into account how their treatment would affect their relationships with others, specifically pleasing family members.

As indicated by the definition of identity described above, social relationships are a factor in identity formation, particularly in this age group, so prioritizing interpersonal relationships as such a strong motivation to change behaviour is not surprising. Almost separate from the extent to which medication seems to make the patients themselves feel better, they note concern that at least others observing them notice an improvement (Floersch et al. 2009). Based on this finding, this reliance on the opinions of others may be related back to the desire to be ‘normal,’ which is relative to the sociocultural context within which an individual lives. As discussed in Chapter 3, normality is the similarity to the average experience of others in the same population as determined, for example, by age, geography, socioeconomic status, and so on. To be normal, then, is to be perceived, by oneself and others, to fall within the mainstream experience. Hence, it may be suggested that the adolescents’ expectation that their medication will enable them to approach normality is

actually more dependent on others' perception of the medication's effect than their own perception.

Taking into account the effect of others' influence on paediatric psychiatric treatment, for more effective care, Dilallo and Weiss (2009, p. 108) suggest 'motivational interviewing' to improve adolescents' receptiveness to treatment and help them develop stronger identities. The authors emphasize the relationship and rapport between the clinician and paediatric patient, and the importance of the clinician having a full understanding of the patient's context both prior to and following the prescription of medication. 'Motivational interviewing' is the term coined to describe this style of practice, and is defined as:

An efficient and collaborative style of clinical interaction that can boost the effectiveness of the therapeutic alliance by enhancing three major elements: empathy that is accurate to the patient's experience, patient confidence in his or her ability to improve, and positive expectations regarding the recommended treatment. (Dilallo & Weiss, 2009, p. 108)

The therapeutic alliance is a reference to the interaction between patient, parent, and clinician in the context of paediatric care. This approach incorporates both awareness of identity development and expectation for treatments. Dilallo and Weiss (2009) note that originally, motivational interviewing was presented as a treatment strategy for substance abuse in adults and later adolescent adherence to type 1 diabetes treatment, but it has been modified for adolescent psychiatric treatment by addressing behavioural problems as 'potential targets for change' (Dilallo & Weiss, 2009, p. 109), which are within the ability of the patient to develop control through improved self-awareness. Responsibility for change is placed on the adolescent patient and away from the clinician and parents, recognizing the patient as the centre of control. To effectively motivate change, then, the clinician must first evaluate the patient's initial understanding of his or her condition in order to determine the best way to communicate a treatment plan that the patient will best be able to adhere to based on such an understanding of his or her own needs. It is a non-confrontational approach that provides

paediatric patients the necessary treatments while also providing opportunity for them to experience their own autonomy and develop a stronger sense of who they are (Dilallo & Weiss, 2009).

4.6 In summary, what are the most prevalent ethical concerns in regard to the psychological implications of psychiatric diagnosis and treatment within the paediatric population, particularly in the case of paediatric depression?

As discussed in this chapter, the following ethical issues arise when treating children for psychiatric disorders. Since children are not fully developed psychologically, their experience of their disorder is unique compared to that of adults; children are still integrating experience and their own reaction to experience into an understanding of themselves. This difference from adult experience, as indicated by the difference in prevalent symptoms, needs to be considered in order to make an appropriate diagnosis because it affects children and adolescents' process of developing an identity and coping abilities. Further, whether the existing diagnoses are suitable for the paediatric population or whether they require revision should be considered, particularly as psychiatric diagnoses have such a significant effect on the development of identity at this age. The impact a diagnosis has on a child or adolescent patient who is only just developing a concept of self is noteworthy not simply as a means of determining the appropriate treatment plan, but also because it will leave a lasting effect on how the patient perceives him or herself in relation to the world in which he or she lives. What follows the effect of diagnosing, then, is the impact that the treatment will have on the paediatric patient's concept of self. Taking medication or even cognitive and behavioural therapy will cause patients to alter their thinking, including thoughts about themselves, which will have a more significant consequence and meaning to those individuals (paediatric patients) who do not yet have a stable understanding of who they are, versus adult patients

who already have a more developed sense of themselves. This influence may have both positive and negative effects on the development of self-understanding.

In the case of paediatric depression, for example, a number of questions concerning the psychological development of the young patient arise. Prior to making a formal diagnosis, it must be determined if the individual's symptoms are truly outside normal child experience. Once the diagnosis of depression has been given, how does the child or adolescent incorporate this label into his or her understanding of self? Is the depression part of who he or she is internally? Is it simply something that affects him or her but is separate from him or herself? Is the child so young that he or she does not understand what 'depression' is and/or has not developed any meaningful concept of self yet? Based on the information presented in this chapter, diagnosing children and adolescents with depression may have various levels of impact depending on each individual patient, how long he or she has been experiencing the disorder, how old he or she is when given the diagnosis, and where he or she is in terms of understanding his or her own identity. In terms of treatment, then, how does a patient's understanding of him or herself change as compared to before beginning treatment? Can he or she interact with peers and family members more effectively having received antidepressant treatment? Has treatment made the individual feel more 'normal' (either more emotionally stable and/or better aligned to the perceived mainstream experience)? Does he or she feel more in control of his or her mood and behaviour? How much of the individual's behaviour does he or she attribute to the medication? Again, the effects of medication on the child's understanding of self and perceived autonomy varies by individual, and is dependent on the level of development the patient has reached at the time of treatment as well as his or her receptiveness and reaction to the medication. This population is in the process of developing their individual identities, and by providing a

diagnosis and treatment, more complex factors are added to this process outside the ‘normal’ experience.

CHAPTER 5

What does paediatric depression mean in terms of neurodevelopment?: A biological perspective

5.1 What is the expected brain development during childhood and adolescence?

Before addressing the differences in development of individuals with a disorder and/or undergoing treatment, it is important to identify normal brain development. At an age when the brain is already subject to significant changes, which research is only just beginning to be able to describe and understand, it is difficult to predict the effects psychiatric experience has on the young brain and its development. Following prenatal development of the neural tube into the brain, ventricles and spinal cord, and the migration and scaffolding of glial cells to form the cortex, rapid programmed cell death occurs over the last few months of gestation into the first month of postnatal life, resulting in the loss of approximately half of the individual's neurons. Simultaneously, synapses are proliferating and organizing, a process known as synaptogenesis, which peaks around age two, when the brain has about one and a half as many synapses as an adult brain. Elimination of certain synaptic connections follows synaptogenesis, a process that varies in rate across different brain regions and continues into early adulthood. Further, myelination also begins prenatally and continues into early adulthood. The myelination process follows an inverted U pattern, starting in the brain stem and progressing in the anterior direction toward the prefrontal cortex, and moving from inferior, proximal, sensory, and projection pathways toward superior, distal, motor, and association pathways (Coghill et al., 2009).

Investigating brain development in ages 5-22 years, the National Institute of Mental Health (NIMH), within the National Institute of Health of the U.S. Department of Health and Human Services, has undertaken a paediatric development mapping project. Through a large sample of magnetic resonance imaging (MRI) scans taken every 2 years of both healthy and

disordered children, data are beginning to describe key brain changes over the course of development in the paediatric population. The findings published thus far indicate:

- Total cerebral volume peaks at 14.5 years in males and 11.5 in females with the brain being 95% of this peak by 6 years
 - Male brains are approximately 9% larger than female brains
 - Lateral ventricular volume continues to increase across the age span
 - Cortical grey matter volume follows an inverted U developmental course. The volume, however, peaks at different times in different regions [...] When mapped in more detail there are distinct patterns of development seen within these specific brain regions. For example, the dorsolateral prefrontal cortex (important for impulse control and decision making) is particularly late to reach adult thickness
 - There are gender specific differences in the amygdala and hippocampus grey matter with amygdala volume only increasing with age in males and hippocampal volume only increasing in females
 - In contrast to the grey matter, white matter volume increases throughout childhood and adolescence
- (Coghill et al., 2009, p. 37)

Given this research, it is no surprise that the overall plasticity of the child and adolescent brain leaves individuals at increased risk for psychiatric disorder. It would also seem that more research in this area may help correlate the findings above with gender differences in prevalence of different disorders.

It may be possible to start tracing such developments by studying slow-wave activity (SWA) through sleep studies, as it has been found that changes in SWA patterns, indicating depth of sleep, appear to reflect trends in brain development (Kurth et al., 2010). Kurth et al. (2010) present novel research correlating brain plasticity and remodeling with SWA during sleep through the developmental ages of 2.4 to 19.4 years of age. In agreement with the developmental changes noted above, ‘the main finding shows that the location with maximal SWA undergoes a shift from posterior to anterior regions across childhood and adolescence’ (Kurth et al., 2010, p. 13216). Further, the resulting inverted U-shaped course of SWA over

time reflects the development of synapse density and pruning, as well as synaptic strength and regional maturation. Generally, the study demonstrates patterns of SWA mirroring anatomical and behavioural development:

Our anatomical localization of maximal occurrence of SWA revealed that, first, the maxima occurs over occipital lobe in preschoolers, followed by parietal regions and posterior frontal lobe in school-age children (from 8 to 14 years) and, finally, the SWA maxima spreads to frontal lobes during adolescence. Young and older adolescents (after ~14 years of age) present a frontal predominance of SWA [...] not yet as pronounced as in adults. (Kurth et al., 2010, p. 13216-7)

With these noted correlations between measurable sleep patterns and otherwise known brain development, this study seems to present a feasible method of observing brain plasticity, and Kurth et al. (2010) suggest using such sleep studies as a tool for detecting abnormalities that may lead to psychopathology in the paediatric population.

Another recently proposed method of brain development tracking is detailed by Shen et al. (2010), using MRI-reconstructed 3D neuroimaging as an efficient, cost-effective, and precise clinical tool to measure brain volume, and by extension, brain development. This technique shows changes in grey, white, and total brain matter volume, and also allows visualization of ventricles, vessels, and pathological lesions. Investigating the normal brain development of children ages 3 months to 12 years and 11 months old, the study suggests that grey matter grows primarily until age 4, and white matter increases from birth through adolescence. The results found by this study parallel previously collected data showing myelination and synaptogenesis processes during early life, so this procedure may provide physicians a plausible method of observing and evaluating brain development and more easily detecting abnormalities in the clinical setting.

5.2 More specifically, are there neurosystems that are particularly plastic and/or vulnerable at this stage of development?

As discussed in the previous chapters, emotional, social, and psychological development are very significant experiences during childhood and adolescence, but what are the underlying brain developments reflected by these experiences? In terms of the influence of brain development on identity formation, findings outlined by Feinberg (2010) suggest key regions in the brain associated with self concept, specifically the frontal, medial frontal, medial and orbitomedial prefrontal cortices. It is not surprising, then, that as children and adolescents develop their sense of identity, the prefrontal cortex is a region undergoing dramatic change through childhood into early adulthood. In the study conducted by Feinberg (2010), results of different brain lesions were used to determine ‘neuropsychologies of the self’ (NPS), which ‘are a group of conditions in which a brain lesion causes a profound and specific alteration in the patient’s personal identity or personal relationships between the self and the world’ (p. 75). Feinberg describes three categories of NPS identity disorders: those of the bodily self, the perceived constraints of one’s physical body; those of the relational self, the interaction and perceived significance of oneself in the context of one’s environment; and those of the narrative self, one’s understanding of their past and present experiences. Feinberg (2010, p. 76) remarks,

NPS differ from purely cognitive conditions [...] in that these [cognitive] conditions are *neutral* with reference to the individual’s relatedness to the self and the world in contrast to NPS which are specifically related and in many cases restricted to something of *personal significance* to the individual.

Based on this theory, if these regions of the prefrontal cortex are affected by abnormalities of a disorder and/or by treatment, then effects on identity should be expected. Therefore, it is understandable that psychiatric conditions concerning identity are particularly meaningful to individuals, perhaps even more so in young individuals whose identities are still developing.

As such, experiences related to the disorder and treatment may be more likely to be a greater factor in a patient's developing concept of self than a language disorder, for instance.

Further, the prefrontal cortex is also involved in emotional development, especially during adolescence, as is the amygdala and the connections between these two regions (Perlman & Pelphrey, 2011). Problem-solving involving motivation and regulation of affect, which are those circumstances that elicit emotional responses, activate the ventral and medial prefrontal cortex (VMPFC) as well as the amygdala, and during childhood and adolescence individuals develop connections between, and regulation of, these brain regions. The amygdala is believed to detect emotionally relevant stimuli, while the VMPFC appears to control emotional response; however, as discussed above, the prefrontal cortex (PFC) is one of the last brain regions to complete development into early adulthood. Thus, as the VMPFC and its regulation of emotional response to stimuli activating the amygdala continue to change through childhood, temperament and emotion can be expected to be less controlled during adolescence. In their study of PFC-amygdala connectivity during emotionally driven problem solving tasks, Perlman and Pelphrey (2011) demonstrated that in both children and adults during heightened negative mood amygdala activation increases, and over lasting periods of negative mood the connectivity between the PFC and amygdala also increases. The study also showed that effective connectivity from the PFC to the amygdala increased with increasing age through childhood, meaning the activity in the PFC has increasing impact over the activity in the amygdala as development progresses.

In addition to this emotional development, puberty and the changing of hormone balance greatly affects both brain structure and function, which allows affective and social brain systems to develop (Forbes & Dahl, 2010). Puberty has a dramatic effect on what Forbes and Dahl (2010, p. 67) term the 'social re-orientation of adolescence,' which includes organizational effects at the cellular level in the brain, such as testosterone's effect on the

growth of white matter, direct behavioural effects, and influence on experience. The authors of this study call attention to the higher correlation of puberty rather than age to changing behaviour and motivation during adolescence, such as sensation-seeking tendencies, increased risk behaviours and increased social concerns, such as those pertaining to peer pressure, social rejection, popularity and status, developing friendships, romantic relationships, and sexual relationships. A greater understanding of the connection between social and neural development is required, particularly as dysregulation of emotional and behavioural control has led to ‘the *health paradox* of adolescence’ (Forbes & Dahl, 2010, p. 66). This is described as the notion that adolescence is a time of great physical health, but also has twice the morbidity and mortality rates than other periods in life. This suggests that as adolescents begin to develop long-term behaviour patterns, puberty may be linked to an increased risk of emerging affective disorders and psychopathology.

5.3 How does neurodevelopment affect psychopathology? Why is the paediatric population at higher risk than adults for many psychiatric disorders?

As described above, the structure and activity of the brain are changing drastically during childhood and adolescence. Paus, Keshavan, and Giedd (2008) review why mental health disorders appear to peak during adolescence (approximately 14 years of age). Grey matter increases until puberty, and then begins to decline, as reflected in the inverted U-shaped developmental pattern; whereas, white matter continually increases from childhood through early adulthood. While less understood, functional changes through development are mostly noted in relation to executive functions, which include planning, decision-making, emotion and behaviour regulation, sensation-seeking and risk-taking. The underlying mechanisms of these changes are proposed, such that ‘the apparent loss of grey matter reflects an increase in the degree of myelination of intra-cortical axons’ and other changes in

axonal calibre to account for the increase in white matter (Paus, Keshavan & Giedd, 2008, p. 949). Furthermore, the development of neural connectivity between different regions of the brain appears to correlate to social development, measured by resistance to peer influences; stronger connections are associated with lower influence by peers. This is indicated by three neural networks: the ‘action-observation network,’ imitation processing by mirror neurons; the ‘biological-motion processing network’ or ‘superior temporal sulcus (STS) network,’ processing of social cues; and the ‘executive network,’ cognitive processing, decision-making and memory (Paus, Keshavan & Giedd, 2008, p. 950).

Using schizophrenia, substance abuse, and affective and anxiety disorders as examples, Paus, Keshavan and Giedd (2008) highlight that adolescent brain development puts individuals at risk for psychiatric disorders due to the vital changes the brain experiences as described, particularly when looking at how/when these changes occur. Overall, the development of psychopathology appears as a result of interacting genetic and environmental factors. Schizophrenia has been observed as exaggerated synaptic elimination, which may be influenced by both biological and external stress in early life. It has been suggested that substance abuse may be the combination of over-sensitive reward circuitry, particularly in the nucleus accumbens, and less aversive activation of the developing GABA_A receptor, and results in inhibition of NMDA receptors, particularly in the adolescent hippocampus.

Lastly, and of particular relevance to this project, affective and anxiety disorders, including major depression, have been associated with abnormal brain activation in relation to social and emotion processing, which is also reflected by ‘reported structural anomalies in the superior temporal gyrus, the ventral prefrontal cortex and the amygdala’ (Paus, Keshavan & Giedd, 2008, p. 953). These affective disorders also show interesting gender differences, from nearly equal prevalence rates between genders in early life to approximately twice the prevalence in females to males after puberty. Due to this trend, the prevalence difference

may be linked to changing hormones during and after puberty, particularly the stress-related steroid tetrahydroprogesterone (THP), which activates the hippocampal $\alpha 4\beta 2\delta$ receptor located in the CA1 region and has been associated with increased anxiety (Paus, Keshavan & Giedd, 2008).

However, this proposed mechanism associated with increased risk to affective disorder, along with other pathophysiology associated with paediatric development of psychiatric disorders require more investigation. As Paus, Keshavan and Giedd (2008) indicate, any anomalous timing or magnitude of the changes experienced by the developing brain put individuals at risk of disorder, so it is important to gain a better understanding of not only *what* but also *how* these changes are occurring. With that in mind, Ziermans et al. (2010) investigated potential markers in brain development that may indicate the development of psychosis. Consistent with the information pertaining to schizophrenia development above, by following high risk individuals through development, Ziermans et al. (2010) found that adolescents at high risk for psychosis who eventually developed psychosis by the 2-year follow-up evaluation showed an exaggerated decline in total brain volume, reduced growth of white matter and significant cortical thinning. Similar developmental research for other psychiatric disorders may allow for detection of specific brain changes and earlier intervention in psychopathology. Though, with increasingly early intervention, more research also needs to investigate psychotropic treatment in the paediatric population.

5.4 What are important factors to be considered when treating children with psychotropics that differ from treating adults in terms of neurobiological effects?

Based on the evidence presented here, the paediatric brain is particularly vulnerable to the risk of developing psychopathology, but this time of increased plasticity likewise presents unique responsiveness to psychotropic treatments. While the evidence of long term effects

and safety of psychotropic drugs on the developing brain continue to build, the increase in diagnosis and prescription treatment for psychiatric disorders in children far overstretches the progress being made in the research data. Further, an even greater disparity between the lag in research and actual prescription prevalence exists in combined pharmacology, as children are often diagnosed and treated for comorbid disorders (Wilens, 2009). Carlezon and Konradi (2004) review what is understood of the link between behaviour and biological effects of psychotropic drug treatment. The authors note the possibility of emerging public health issues with the increased consumption of psychotropic drugs, as well as caffeine, earlier in life, as the young developing brain experiences changes inflicted by treatment that result in long lasting adaptations that may or may not be beneficial to the individual.

With repeated exposure to psychotropic drugs, levels of responsiveness change either by increasing tolerance or sensitization, that is reaction to drug effects show a progressive decrease or increase, respectively. What Carlezon and Konradi (2004, p. 48) term ‘exposure-dependent’ adaptations are of concern due to their role as precursors to addictive behaviours. Furthermore, repeated exposure is associated with molecular alterations in the brain, causing changes in gene and protein expression. More recently, research is beginning to describe how these molecular effects are connected to behavioural effects of drug treatment, for example linking CREB activity in the nucleus accumbens (NAc) shell to depressive behaviour as demonstrated by the work of Turgeon, Pollack and Finch (1997), Pliakas et al. (2001), Barrot et al. (2002), and Carlezon et al. (1998) (cited in: Carlezon & Konradi, 2004).

Using methylphenidate exposure during early development as an example study, Carlezon and Konradi (2004) discuss how the exposure-dependent changes that are explained in adults with regard to behaviour-molecular models may be completely different in children, though paediatric results are also considerably inconsistent. In terms of behaviour, it is undeniable that early exposure to neurostimulants alters responsiveness to stimulants later

and their rewarding effects later in life, though it is debated whether these alterations are an increase of tolerance or sensitivity to drug effects. When investigating the molecular effects of early methylphenidate exposure, rat subjects showed increased CREB expression in the NAc shell later in life, which is associated with depressive behaviour; this contrasts the neuroadaptation associated with stimulant exposure in older subjects, which is linked to addiction risk. This is suspected to only be one of many neuroadaptations of early stimulant exposure; other brain regions require closer investigation in this regard. Similar studies of the molecular effects of other psychotropic drugs are also needed.

There have been studies conducted to determine clinical effects of other psychotropic drugs for paediatric use. Alacqua et al. (2008) interpret retrospective clinical charts reviewing the use and tolerability of antipsychotics and antidepressants to highlight prescribing trends and identify safety and reaction concerns in the paediatric population. The study included the atypical antipsychotics risperidone, olanzapine, uetiapine, and clozapine, and SSRIs paroxetine, sertaline, citalopram, and fluoxetine, but this study only looked at the effects over the first three months of treatment. Antipsychotics were found to be prescribed mainly to treat psychosis and autism, and conduct disorder and mental retardation to a lesser degree, with the highest number of prescriptions for risperidone and olanzapine. However, nearly one third of subjects in the study discontinued treatment within three months due to adverse drug reactions, and only a minority of subjects reported major improvements during treatment. The majority of SSRI prescriptions were indicated for OCD, anxiety disorder, and conversion disorder, with a few cases used for panic attack and conduct disorder. While almost half of subjects saw no improvement or worsened condition with treatment and approximately 20% experienced adverse effects, none of the subjects discontinued treatment within the first three months that were studied. Alacqua et al. (2008) carried out their research in southern Italy; however, their results were consistent with previous studies

conducted in the U.S. It is interesting to note that SSRIs are not indicated to treat depression, but other disorders. Further, at the time of this study both the FDA and EMEA were beginning to release warnings against the use of SSRIs in children with the exception of fluoxetine (in the US, this exception was extended to include sertraline and fluvoxamine indicated for OCD, as well; see Chapter 2), yet fluoxetine was the least prescribed SSRI in this study.

Looking specifically at antidepressant treatment in children and adolescents, Moreno et al. (2007) examined the literature through a systematic database search of both electronic and specialized collections, including published and unpublished information available to the public. Their search determined that many drugs provide positive results, meaning treatment proved more effective than placebo, in the adult population, but that few studies have published positive results in children and adolescents; thus, antidepressants still lack efficacy for use in the paediatric population overall. The study covered trials with TCAs, SSRIs, and other newer antidepressants, including venlafaxine, mirtazapine, and nefazodone.

Moreno et al. (2007) propose a number of possible explanations for the efficacy differences between paediatric and adult populations. TCAs may be less effective in children due to the noradrenergic neural system developing into early adulthood, and the neural changes related to puberty increase the risk of mania with the use of SSRIs nearing the age of 14, after which mania is a more common risk with the use of TCAs. In addition to these mechanistic findings, pharmacokinetics and pharmacodynamics, or the interactions between the drugs and youth physiology, are discussed. Prior to puberty, young people have notably faster metabolisms, different water distribution in the body, as well as lower body fat concentration, and as a result, children may require higher, more frequent doses of medications metabolised in the liver, such as antidepressants and antipsychotics, to see effective results. With regard to antidepressant metabolism, the authors note:

As antidepressants have two to three times shorter half-lives in youngsters, they need to be administered more often than to adults to avoid withdrawal symptoms between doses that can be wrongly interpreted as the absence of an adequate response with the exception of fluoxetine, which has a longer half-life. Other factors, such as reduced drug protein binding and a more permeable blood-brain barrier in children, also play a role and increase drug availability. (Moreno et al., 2007, p. 189)

Despite this knowledge, most clinical trials have only been carried out with adult subjects, hence the off-label prescribing practices. Furthermore, it has been suggested that depression is heterogeneous, meaning the risk of developing depression increases in newer generations who have depressed parents. Also, paediatric versus adult depression presents different biological signs and drug responses, including variation in placebo response, which may require a different approach to treatment. With regard to placebo response, both Moreno et al. (2007) as well as Shearer and Bermingham (2008) note that research often shows that children respond comparably well to the placebo treatment as to SSRI treatment. These data indicate the importance of further studies of child-specific efficacy.

5.5 What are some necessary methodology considerations and directions for future research?

The combination of lacking clinical data and continuation of off-label treatment practices indicate an obligation for future research in order to find the safest and most appropriate treatment for children with psychiatric issues. In terms of future directions, Carlezon and Konradi (2004) review what data exists already and suggest that the following should be addressed:

One, to examine whether other classes of psychotropic drugs produce the same types of effects; two, to use more complex behavioral models to examine how these agents affect high level motivation and cognitive function; and three, to examine if there are periods of development in which it is particularly safe or risky to use psychotropic drugs. (p. 48)

Prior to clinical trials in humans, animal research models are discussed by Carlezon and Konradi (2004). Especially in paediatric studies, it is difficult to find an appropriate model to represent human brain development. Even in humans, the boundaries of childhood, adolescence and adulthood are variable, so applying parallel limits to animal models is even more challenging. Moreover, animal models, typically rats, differ in the way they metabolise and react to drugs, particularly during development and with regard to psychiatric conditions. These factors make it difficult to measure appropriate dosages, as well as to uncover the differences of treating normal individuals, individuals with an underlying pathology and individuals with a known psychiatric disorder when trying to apply animal models to paediatric practice in humans.

When designing clinical investigations with regard to antidepressant treatment in children, then, many variables need to be taken into account, as discussed by Moreno et al. (2007) as well as Vasa, Carlino and Pine (2006). Firstly, diagnosis of child depression is subjective, as discussed in previous chapters, and there is no consistent tool of assessment for making the paediatric diagnosis. Secondly, both comorbid disorders and polypharmacy practices make treatment results difficult to interpret; thus, the specific effects of antidepressants on paediatric depression will be unclear, but with the high rates of comorbidity and polypharmacy, an understanding of the resulting interactions also requires more research in itself. Thirdly, different subtypes of depression may respond to psychotropic treatment differently, as indicated by different biological signs that have been studied previously; another important difference concerns distinguishing early onset of bipolar disorder (BPD) versus major depression because treatment, particularly with SSRIs, may aggravate manic symptoms in young undiagnosed BPD patients. Lastly, inconsistencies in study design, as well as which studies are published, make it nearly impossible to compare

results between research projects, particularly when studies have limited sampling which may not be applicable to the entire population.

In Germany, Austria, and Switzerland, Mehler-Wex et al. (2009) suggest Therapeutic Drug Monitoring (TDM) as a method of more widespread data collection of psychotropic drug effects, including polypharmacy, as they appear in actual clinical practice in this population without carrying out unnecessary and excessive research. TDM would closely monitor plasma/serum levels and side effects in treated patients at the time of treatment, and thus the dosages and treatment plan could be better tailored to the individual patient. At the same time, this data would be entered into a network to build a database to support future treatment plans (Mehler-Wex et al., 2009). Such a database would remove the challenges of variability in applying clinically controlled research to real clinical practice, and it would provide a much larger, fully representative sample of results.

5.6 What legislation is in place to improve research and prescription safety for paediatric patients? Why is paediatric protection vital?

While doctors provide care in the best interests of their patients, it has already been highlighted above that holes of uncertainty remain in current medical treatment. What legislation is in place to protect child/adolescent safety? Since this population is especially vulnerable, what specific measures have been made to ensure their needs are met? As outlined by Auby (2008), the following legislation has passed in the US with respect to paediatric medication: Pediatric Labeling Rule (1994); Modernization Act (1997); Pediatric Rule (1998); Best Pharmaceuticals for Children (2002); Pediatric Research Equity Act (2003); and amendments to the Pediatric Research Equity Act (2007) and Best Pharmaceuticals for Children Act (2007). Overall, these pieces of legislation encouraged

drug studies for the paediatric population by providing incentives for pharmaceutical companies.

In the midst of the above legislation, the US Surgeon General, Dr. David Satcher, held a conference to highlight the growing mental health needs of children and adolescents and to present suggestions for future direction in the nation's attempt to address such needs (US Public Health Service, 2000). There were eight major goals set for the conference:

1. Promote public awareness of children's mental health issues and reduce stigma associated with mental illness.
2. Continue to develop, disseminate, and implement scientifically-proven prevention and treatment services in the field of children's mental health.
3. Improve the assessment and recognition of mental health needs in children.
4. Eliminate racial/ethnic and socioeconomic disparities in access to mental healthcare.
5. Improve the infrastructure for children's mental health services including support for scientifically-proven interventions across professions.
6. Increase access to and coordination of quality mental healthcare services.
7. Train frontline providers to recognize and manage mental health issues, and educate mental health providers in scientifically-proven prevention and treatment services.
8. Monitor the access to and coordination of quality mental healthcare services. (US Public Health Service, 2000, p. 4)

These goals were attended to by dividing the conference into three panel discussions: 'Identifying, Recognizing and Referring Children with Mental Health Needs'; 'Health Service Disparities: Access, Quality, and Diversity'; and 'State of the Evidence on Treatments, Services, Systems of Care and Financing' (US Public Health Service, 2000, pp. 16, 27, 32). While the goals outlined do adequately address the major difficulties present in current paediatric psychiatry, achieving them in the immediate future may be too idealistic; the aims focus on both system and social issues which are large enough problems that it will be years before any changes will impact care. Following the press release of this conference, in 2001 the American Psychological Association put together a report in response, which

outlined strategies to achieve the goals set by the Surgeon General's conference. The association then created a task force in order to carry out those strategies as addressed by five key points:

1. Promoting public awareness of children's mental health issues;
2. Improving the infrastructure to address funding and parity issues;
3. Increasing access and coordination of quality mental health services;
4. Training providers about child development and mental health; and
5. Monitoring access and coordination of quality mental health care services.' (American Psychological Association, 2001, p. 12).

The task force serves to ensure the continuing advocacy of these strategies in mental health practice as well as policy creation and revision. Though the task force has put forth realistic strategies, again, significant changes in care may be expected to progress slowly.

Based on the previously instated US regulations, the EU passed Regulation (EC) No 1901/2006 in 2006. Prior to this legislation, Lehmann (2008, p. 1) notes, 'The legal framework for conducting clinical trials, including children/minors, is set up in Directive 2001/20/EC, the Clinical Trials Directive (CTD), for the European Union (EU).' Rocchi et al. (2010) discuss why there was a need for further regulation in the EU. With the growing prevalence of off-label prescriptions for the paediatric population, the conflict intensifies between conducting paediatric research and the problem of medicating children without supporting experimental data. On the one hand, it is costly and ethically problematic to carry out many paediatric studies; however, this is counterbalanced by the issue of prescribing untested dosages of drugs to children. The new regulation specifically covered vulnerable populations, addressing research requirements, rewards, incentives and penalties, shared access to collected data, and providing appropriately tested medicines to be used in child populations (Auby, 2008; Lehmann, 2008; Rocchi et al., 2010). Auby (2008) explains the

contrast to the US legislation, in that the new EU regulation encouraged more proactive development of paediatric medications, key points being increased quality research and information availability through the European Paediatric Committee (PDCO) and Paediatric Investigation Plan (PIP). The PIP is a required development plan outlining paediatric application for all medicinal product research (unless the product is proven to treat adult-only conditions, as determined by the PDCO), and must be submitted to and approved by the PDCO, which includes members representing each EU state as well as three healthcare professionals and three patients' association representatives (Auby, 2008; Rocchi et al., 2010). While the influence of pharmaceuticals and its associated consumer market are not as notable as in the US, the industry does have considerable power in research across the world. Stoyanova-Beninska et al. (2010) propose that prior to the new EU regulation, paediatric research was lacking in part because there was little incentive for pharmaceutical companies to pursue such studies, and also due to the belief that paediatric psychopathology was mainly external and treatable through non-medicinal methods. However, they further suggest triggers for regulation were the concern that adult data could not, in fact, be extrapolated to children, as found with SSRIs and increased suicide risk in adolescents, and that drug treatments in children needed more intense investigation (Stoyanova-Beninska et al., 2010).

To support the collection of more experimental data within the new EU regulations, Manolis and Pons (2009) suggest model-based studies to minimize the number of necessary trials conducted in children in order to test safety and efficacy of drugs. By definition:

Modelling and simulation (M&S) is a methodology widely used to support drug development. Modelling is the science of using mathematical language to describe and quantify a system. Simulation refers to the use of these models to make quantitative predictions. (Manolis & Pons, 2009, p. 494)

If this method is employed correctly, it may be a way of increasing practical data without having to carry out many tests in children. However, the authors make the important note

that it cannot replace human trials as it is only based on assumptions and parallel adult data, but it can provide supplemental data to support fewer paediatric trials.

5.7 In summary, what are the most important ethical issues with regard to neurodevelopment and psychiatric treatment, particularly the use of antidepressants?

As discussed in this chapter, the human brain continues to develop through childhood into early adulthood. While more research is required, emerging evidence suggests that the neurosystems underlying the development of identity, emotional control, and social integration are considerably plastic until the third decade of life, resulting in an increased risk of developing psychopathology during this time. Any deviations from healthy neurodevelopment with regard to how or when neural changes occur have the potential to produce a substantial impact and disorder. Depression, for example, may be linked to abnormalities in the superior temporal gyrus, ventral prefrontal cortex, and amygdala, which present as atypical development of social and emotional processing. This is consistent with the neurodevelopment data described above. Additionally, with the differences observed in depressed individuals' prefrontal cortex, it would not be surprising that this disorder may also affect identity formation.

In terms of introducing psychotropic drugs to the developing brain, then, the different physiology of children from that of adults in addition to neural plasticity must be considered. Firstly, children will metabolise drugs differently than adults, as described in the chapter above. Secondly, heightened plasticity in the brain lends to more significant neuroadaptations with respect to drug responsiveness, i.e. tolerance and sensitization, which may leave extensive lasting effects. Specifically in the case of antidepressant use in the paediatric population, overall the research lacks positive results, despite findings in the adult population. There are numerous policies and legislation in place to protect children against

unsafe treatment and unnecessary research testing, but without clinical trials safety data will remain lacking. Moreover, it is particularly challenging to find appropriately matched models that can reflect both human brain development and psychiatric conditions/treatment practices as they appear in the clinical setting prior to conducting clinical trials. Through the combination of such methods suggested in this chapter, namely TDM and M&S, widespread and minimally invasive sample data reflective of actual clinical presentation and practice may be collected and analysed. Future studies may then indicate the most appropriate prescription practices for psychotropics such as antidepressants in the paediatric population in hopes of diminishing off-label prescription prevalence.

CHAPTER 6

What is the context of paediatric depression around the world?: A cultural perspective

6.1 What do mental health services look like around the world?

Having focused on psychiatric practices in the US and UK up to this point, what is the global context for paediatric psychiatric care? In 2005, the WHO published the *Mental Health Atlas* as part of the Atlas project, compiling data on available mental health resources across the 192 Member States. Overall, despite finding a global awareness of a substantial mental health burden, there is a severe lack of available resources in the majority of countries across the world. Looking at the child-specific data from 186 of the Member States, defining children as ages 0-14, 62.4% of the countries showed any child-specific mental health programmes. When comparing the percentage of countries in a geographic region with the presence of child mental health programmes to the percentage of child population, Africa, the region with the highest proportion of children (42.6%), had the lowest percentage of countries with paediatric mental health programmes (37.0%); conversely, the Americas and Europe, the regions with the lowest proportion of children (30.4% and 19.1% respectively), had the highest proportion of countries containing mental health care facilities for children (81.3% and 77.6%, respectively; see Table 6.1). In terms of income stratification by country and the presence of paediatric mental health services, the percentage of countries with available services were proportionate to the income of the country, i.e. a higher percentage of wealthier countries have mental health care services for children than lower income countries (WHO, 2005a).

As another part of the Atlas project, the WHO provides a more extensive analysis of global paediatric mental health care in the *Atlas: Child and Adolescent Mental Health Resources* report (2005b). However, this document contains information from only 66 of the

192 Member States based on data collected from questionnaires that were completed by key informants in each country, and excludes data from the US, Canada, France and Australia (see Appendix E). While representing less than half of the Member States, the data present some critical information. Globally, about 20% of children and adolescents are affected by mental disorders, 4-6% of whom are significantly distressed and require clinical intervention. With the exception of the Western Pacific region, regional presence of mental health programmes reflected the same trend as described above, but in this limited sample the percentage of countries found to have such programmes appeared much lower for some regions while higher for others. This shift indicates that in Africa, the Americas, the Eastern Mediterranean, and Europe many countries that claimed to have mental health care programmes when surveyed for the original *Mental Health Atlas* chose not to participate in the survey for the specific *Child Mental Health Atlas*, while many countries in the Western Pacific and South-East Asia that did *not* report having special programmes in the original *Atlas* opted out of the *Child Atlas*.³ In the countries that did offer information for the *Child Mental Health Atlas*, the survey also investigated the proportion of countries in each region which have national policies regarding child and adolescent mental health care, and demonstrated that actual mental health care services lag behind the presence of relevant policy (see Table 6.1). These trends are similarly observed when dividing countries based on income group. The authors suggest that the gap between policy and services may be due in part to grouping mental health policies within national policies of ‘human rights, social welfare, child protection or education’ (WHO, 2005b, p. 14).

³ Unfortunately, since the *Atlas* was a voluntary survey, there was no follow up to determine why certain countries chose not to participate in the *Child Mental Health Atlas*.

Table 6.1: Global child mental health care programme and policy distribution. This table compares the proportion of the population under the age of 14, countries with paediatric mental health care services, and countries with national paediatric mental health care policy in the different WHO Regions, while also comparing data from the *Mental Health Atlas* surveying 186 countries and the *Child Mental Health Atlas* surveying 66 countries (WHO, 2005a; WHO, 2005b).

	<i>Mental Health Atlas</i>		<i>Child Mental Health Atlas</i>	
WHO Regions	0-14 years population (%)	Countries with programme (%)	Countries with programme (%)	Countries with policy (%)
Africa	42.6	37.0	6.3	33.3
Americas	30.4	81.3	44.5	77.8
Eastern Mediterranean	34.6	72.7	33.3	100
Europe	19.1	77.6	66.7	95.8
South-East Asia	32.8	54.5	62.5	50
Western Pacific	32.9	50.0	83.3	66.7
World	31.3	62.4		

It is also noted that, ‘nowhere in the world is the documented need for child and adolescent mental health services fully met’ (WHO, 2005b, p. 16). The Child Mental Health Atlas (2005b) indicates the need for a continuum of care, which is a system that offers a variety of services from home-based to school-based to outpatient to hospital inpatient, among others, and states that at present, ‘in only 7 of 66 countries were the elements of essential services identified that could be considered to represent the presence of a continuum of care’ (p. 18). Barriers to care are listed and include lack of transportation, stigma, lack of resources, lack of communication due to language barriers, and lack of public knowledge. Particularly, the lack of resources is apparent when presented with the information that ‘a 1999 survey in the European region showed the presence of a child psychiatrist in countries to range from one per 5,300 to one per 51,800’, and more astonishingly ‘in most countries in the African, the Eastern Mediterranean, Southeast Asian, and Western Pacific regions the presence of a child psychiatrist is in the range of 1 to 4 per million with a few notable exceptions’ (WHO, 2005b, p. 21). Moreover, while more than half of the countries surveyed

indicated that paediatricians provide mental health care, only a small minority of paediatricians have any psychiatric training; on the other hand, most psychiatrists around the world are not trained to work with children and adolescents. It is difficult both to improve the availability of trained professionals as well as increase accessibility to them as financial support for child and adolescent mental health care is mainly provided by temporary, unsustainable sources, such as international grants and patients' private funds, which lack the stability of government funds. Further, there is a significant lack of accessibility to current medication and information regarding relevant psychotropic treatments.

Prior to the Atlas project, the WHO published *Caring for children and adolescents with mental disorders* (2003), which also specifically addressed the mental health needs of children and adolescents, providing the perceived priority disorders, briefly addressing cultural context of diagnosis, barriers to care, interventions and policies, and emerging trends in paediatric mental health care. Designated by typical age of onset, the following mental disorders are of particular concern in the paediatric population worldwide: learning disorders and hyperkinetic disorders (i.e. ADHD) in early childhood; tics (i.e. Tourette's syndrome) in middle childhood; and depression, associated suicide, and psychosis in adolescence. Pervasive Development Disorder, attachment disorders, anxiety disorders, conduct disorder/anti-social personality, substance abuse, and eating disorders are also of significant concern around the world, and require more intensive care than the disorders previously listed. As discussed in previous chapters, it is further emphasised here that despite increasing knowledge of the biological factors involved in mental illness, social/environmental context remains an important component of the equation and should not be discounted.

Extending the impact of environment to cultural context, then, the presentation and diagnosis of any one disorder may demonstrate considerable variability throughout the world. As diagnostic criteria are generally defined based on Western cultural context and may not

apply well to other cultures, the authors suggest that when diagnosing, ‘one should look at *broader categories of disorder* rather than *narrower disease definitions*’ (WHO, 2003, p. 8). Particularly in developing countries, children are often subjected to ‘*difficult circumstances*’ which may produce either reactive disorders or long term impairment, so it is vital to take context into account in order to determine the appropriate diagnosis/level of impairment so that the child receives the most effective care (WHO, 2003, p. 8).

As expected, the barriers to care discussed above are especially significant in developing countries, but in fact, these barriers are also universal problems. The *Caring for children and adolescents with mental disorders* report (2003) highlights the importance of family communication, awareness and training of adults in the community who work with young people, and developing national paediatric mental health policy as useful interventions to help overcome barriers to care. As evidenced by statistics presented above, there is a universal lack of effective policies regarding child and adolescent mental health care. Having published a report in 2001 with guidance for those countries designing their own policies, the WHO emphasises the necessity for policy, claiming:

The development of child and adolescent health services in the absence of specific national policy leads to: (1) fragmentation of services, (2) inefficient utilization of scarce resources, (3) inability to provide effective advocacy for priority concerns, (4) lack of constituent participation in program development and (5) an inability to incorporate new knowledge in a systematic fashion. (WHO, 2003, p. 14)

Regardless of the status of a national policy, mental health care is becoming a more privatized sector of medicine, which is then balancing more between insurance and managed care than relying on the state for funding and cost/quality control. In theory, the shift toward privatization is to control and minimise costs of care, but without national policy to insure a certain quality of care, access to appropriate mental health care and treatment may easily decline. There is particular concern with regard to medication treatment, as a trend of direct

marketing to patients has been emerging around the world, not just in the West. While patients gather most of their information about medications from the pharmaceutical companies themselves, children and adolescents continue to receive off-label treatment, leading to the ethical dilemma discussed in earlier chapters.

Psychiatric care should be a concern around the world, as Ngui et al. (2011, p. 2) state:

The projected burden of mental health disorders is expected to reach 15% by the year 2020, where common mental disorders (depression, anxiety, and substance-related disorders including alcohol) will disable more people than complications arising from AIDS, heart disease, traffic accidents and wars combined.

In their analysis of the global mental health burden, Ngui et al. (2011) note that less than 30% of the children who require mental health services receive the care that they need. As such, the mental health burden becomes a public health issue sustained by social inequalities, unmet needs, stigma and discrimination, which in turn significantly affects economic development. The correlation between socioeconomic status and mental health disorders becomes self-perpetuating as the lack of advocates and services for the poor continue to widen the gap between healthy and disordered as well as that between wealthy and poor. In developing countries, where mental disorders tend to be much more prevalent, the lack of mental health care policy and access to services means that an estimated 75% to 85% of disordered individuals go untreated. The overall shortage of mental health care workers is paralleled by the migration of these trained professionals away from the developing and rural areas in the most need because there are no structured jobs for them except in developed and urban societies. This further reflects that stigma is not only affecting patients, but also healthcare professionals; medical professionals are often deterred from the mental health field, and in certain cultures more traditional beliefs, including the control of supernatural forces, evil spirits or curses, may leak into mental health practice. Ngui et al. (2011) also

highlight the impact of a global mental health burden on economic development. The cost of effective mental health care is exceeded by the economic loss as a result of mental disorders hindering success. In addition to economic productivity, treating the mentally ill would be expected to result in lower crime rates and more political stability.

6.2 What are some specific trends in services and treatment observed?

A number of reviews regarding regional-specific mental health services and treatment/prescription trends have been consulted from different countries and regions, including Pakistan, Eastern Europe, India, Australia, France, and Western Europe/US. Some regions lag well behind the needs of the population, not just specifically children and adolescents, in terms of public awareness and availability of the most current prescriptions (Pakistan and Eastern Europe, respectively). Other countries have relevant services available but are concerned with the increase in paediatric mental health treatment and prescription trends, and note the need for appropriate ethical guidelines and services (India and Australia, respectively). On the other end of the spectrum, some regions, particularly in the West, are questionably over-treating the paediatric population for mental health disorders (France and Western Europe/US, respectively). However, with a recognised lack of services even in the West, over-treatment may actually reflect an inability of the available services to adequately monitor the treatment that is provided, which is notably not equally accessible by all within these developed countries.

In Pakistan, Zafar et al. (2009) conducted a study to examine public perception of psychotherapy and pharmacotherapy as effective psychiatric treatment. Most of those interviewed in this study supported pharmacotherapy, but it was also made clear that many do not understand the actual meaning of ‘psychotherapy’. In such a society, the general public simply requires more availability of treatment information. It is also important to note,

however, that this survey indicated very little stigma associated with psychiatric care, and the overall results indicate that the ‘general public of the largest city of Pakistan perceive psychotherapy as a clinically effective, cost efficient and acceptable modality for management of mental ailments’, with ‘a significantly greater preference for psychotherapy [...] among younger, females, more educated and financially independent participants’ (Zafar et al., 2009, p. 3). Based on this noted preference, it would be interesting to do future studies to determine a demographic survey of who is receiving psychiatric care in this region, particularly because, despite the positive perception of psychiatric care, the actual resources for mental health care are severely limited in Pakistan.

Looking at an adult demographic, the study by Jordanova et al. (2010) in Eastern Europe presented psychotropic prescribing trends, which remained fairly similar across the five included countries (Albania, Croatia, Macedonia, Serbia, and Romania). In terms of diagnosis, depression was the most frequent in Iasi, Targu Mures and Zagreb, and psychosis was the most frequent in Belgrade, Strumica, and Tirana. Pharmacotherapy findings included polypharmacy as very common even when guidelines often suggested monotherapy, and typically older generation drugs are prescribed (independent of cost). Due to these practices, it may be presumed that the patients in this region experience greater adverse effects; combining treatments may lead to negative drug interactions, and at least in the case of atypical antipsychotics, despite newer drugs being shown not to be significantly more effective, older drugs do have more negative side effects. While antipsychotics and antidepressants are the most common prescriptions, the high prevalence benzodiazepine trends reflect those found in Western Europe. Also, anticholinergics are commonly prescribed in order to offset extrapyramidal side effects caused by typical antipsychotics, which are frequently used in this region. This study did not provide any paediatric data, but as paediatric psychopharmacology trends increase throughout the world it may be assumed

that children and adolescents in this area are receiving some form of psychotropic treatments likely paralleling those trends described for adults.

With the increased prevalence of paediatric psychopharmacology, the need for research in this population is becoming vital, particularly as most children are receiving off-label prescriptions. As paediatric research expands in India, Malhotra and Subodh (2009) raise ethical issues that need to be addressed, particularly informed consent, balancing benefits and risks in research design, and population-specific concerns of conducting research in paediatrics. When discussing informed consent, the authors note three key components. The first is competency, or cognitive capacity to make rational and informed decisions. The second element is information, which should reasonably explain: '(i) the proposed course of treatment, (ii) alternative treatments available, (iii) existence of the potential benefits/potential risks of each treatment options, and (iv) no treatment at all' (Malhotra & Subodh, 2009, p. 22). The third component is voluntarism, the patient's freedom of choice to do what is right for his or her circumstances based on his or her own understanding of the situation and options, values and history, without others' persuasion or coercion. The elements of informed consent are complicated in the case of children and adolescents. For instance, when is the child/adolescent considered competent enough to make their own decisions rather than rely on parent consent? Research has found that from about age 7, children are cognitively competent enough to be involved in decision-making regarding their own care in the form of *assent*, and by age 12 may be competent enough to make their own decisions; though as implied by Chapter 4, cognitive competency is contingent on level of neurodevelopment, which is not precisely defined by age. Based on fluctuations in decision-making abilities in young people, generally independent *consent* is not granted to adolescents until ages 16-18 in the Western world, with few exceptions. Special attention must also be given to particularly vulnerable populations, such as handicapped children, institutionalized

children, patients with chronically progressive and/or potentially fatal disease, and patients in emergency life saving care.

In terms of research design, more scrutinising attention must be given to the predicted benefits outweighing the risks of the treatment in question. Even with regard to placebo treatment, considerations should be made if withholding treatment would incur more potential risks than providing the active treatment. Further risk assessment must be evaluated in paediatrics that may not be as of great importance in adult studies and treatment due to the intensified impact such factors may have on a young patient, including ‘discomfort, inconvenience, pain, fright and separation from parents or familiar surroundings, effects on growth or development of organs, and size or volume of biologic samples’ (Malhotra & Subodh, 2009, p. 27). Finding a balance between potential benefits and risks in paediatric research is further complicated by the ‘inherent paradox of clinical trials in psychiatry,’ balancing the ethical dilemma of treating children and adolescents with untested treatment with the additional ethical challenges of conducting scientific research on treatment efficacy in the paediatric population (Malhotra & Subodh, 2009, p. 27). This review of the issues in paediatric psychopharmacology implies that these are globally identified issues associated with treating children, not simply Western concerns.

Furthermore, Malhotra and Subodh (2009) provide an overview of the clinical paediatric setting in India. As a relatively young, heavily populated country, there is a large paediatric patient population. Culturally, India’s collectivist society typically encourages family participation in patient care, but authority remains largely with the physicians themselves, followed by parental authority, and children are given little to no inclusion in making decisions regarding their care. While written consent by subjects/parents is required for participation in treatment and/or research, lack of education often leads to limited understanding of clinical implications being agreed to. The authors make the following

suggestions for the future: developing a set of ethical guidelines and creating Ethical Review Boards (ERBs), allowing individuals over the age of 14 to grant consent as mature minors and including the community in determining the future of clinical research and practice.

In Australia, McGorry (2007) investigates clinical practice of youth paediatric care and calls attention to the growing need to reform mental health facilities for the adolescents due to the high prevalence of mental health disorders in this population. Including adolescent mental health care within the child sector of psychiatric care is a very recent development in Australia through Child and Adolescent Mental Health Services (CAMHS), and there is a noted misalignment of bridging CAMHS to Adult Mental Health Services (AMHS) for those patients approaching young adulthood. At present, paediatric psychiatry is relatively under-resourced and is addressed mainly through primary care physicians and paediatricians. While CAMHS has made improvements in treating disorders prevalent at younger ages, such as ADHD and conduct disorders, the Australian medical system continues to struggle with the treatment of mental disorders prominent in adolescents and young adults, such as mood disorders, psychosis, and substance abuse. McGorry (2007) suggests reform in youth mental health services for those patients between 12 to 25 years old toward more age-specific services and overlapping care between child and adult services. The author proposes two ways of developing such services:

Firstly, the current system could be restructured and enhanced through a strengthening and extension of the adolescent component of the current CAMHS model. [...] Alternatively, a new stream of care originating at the lower age range of adult psychiatry could be created, as has been established with the early psychosis services developed all over the world in recent years. (McGorry, 2007, p. S55)

Due to the structure of the current Australian system, such reforms are crucial in order to implement appropriate care for adolescents, but it is also an interesting notion that could be applied in other national health systems, as well.

Turning now to countries that have a longer history of medication in the paediatric population, with France's historically high prescription rate, Acquaviva et al. (2009) sought to estimate national trends in psychotropic prescriptions among children and adolescents across the country by looking at specific regional data and comparing findings to other European trends. While overall French psychotropic use is lower than the US, it is similar to that in the UK, Netherlands, and Germany, with a frequency of just over 2% across the paediatric population; however what is being treated and prescribed varies. Methylphenidate is prescribed generally between ages 7 to 16, and has a higher prevalence in males versus females, with a peak in male prescriptions at age eight. Benzodiazepines, SSRIs, and antipsychotics all show prevalence rates increasing with age. More males than females are prescribed benzodiazepines through age 13, and this ratio inverts after age 13. The SSRI female to male ratio is relatively equal until age 13, after which females are prescribed SSRIs twice as much as males. Antipsychotics are always prescribed more for males. There is also a trend of self-medication that does not follow prescriptions, as 'about half of the psychotropics used by young people at 17 years are taken without a decision by a doctor' after acquiring the prescription but not being monitored by a physician or following the indication (Acquaviva et al., 2009, p. 5). This study also highlighted indications for psychotropic medication, noting gender differences as well as other non-psychiatric uses:

Girls use psychotropics to deal with anxiety whereas boys use psychotropics to treat sleep disorders. The use of psychotropics for stimulation or for fun reaches 10% for girls and approximately 15% for boys. [...] It appears that tricyclic antidepressants are used to treat enuresis in children and could be marginally use to treat pain. [...] Methylphenidate has another official indication which is narcolepsy. [...] Haloperidol is used although infrequently as an antiemetic drug. (Acquaviva et al., 2009, p. 6)

Due to the prevalence of self-medication and alternate indications, it is difficult to discern the definite prescribing practices for psychiatric use. What can be determined, however, is that it

is more typical for ADHD to go underdiagnosed and for anxiety-related disorders to be overtreated in France as compared to other nations.

Making the comparison of paediatric psychotropic prescription practices between the Netherlands, Germany, and the US, Zito et al. (2008) found that while there were some small discrepancies among European countries, the most significant difference was between US and the generalised Western European practice. This study investigated stimulant, antipsychotic, antidepressant, and overall psychotropic drug prevalence in patients ages 0-19 for the year 2000, including analysis by age, gender, and concomitant drug use (simultaneous use of multiple psychotropics). Overall, the US showed a much higher prevalence of psychotropic use than the European countries analysed (2.27 and 3.33 times more than the Netherlands and Germany, respectively), and the Netherlands showed significantly higher prevalence rates than Germany. This trend is reflected in the individual prevalence of the antipsychotic, stimulant, and antidepressant drug classes, with fewer disparities among antipsychotic prevalence. However, concomitant use was significantly more prevalent in Germany than in the Netherlands; though, since indication of prescription was not included, the higher trend of concomitant use in Germany may have been due to other factors. Zito et al. (2008, p. 5), note, 'Since the bulk (62%) of the German combinations involved anticonvulsant-mood stabilizer and an anxiolytic/hypnotic, it is not possible to determine the extent of seizure disorder treatment.' While the US did have a higher prevalence of this particular drug combination than Germany, the leading pair combination in the US was stimulants with antidepressants, whereas the leading Dutch pair was stimulants with antipsychotics. The authors suggest that differences in prescribing trends may be influenced by a number of factors, including the use of different diagnostic systems (DSM versus ICD), drug regulations and policies, clinical setting (public versus private care; specialist versus general physician), financial/marketing sources and cultural values.

6.3 What are the global trends for antidepressant prescriptions in the paediatric population?

As mentioned above, paediatric depression is identified as a global issue, but as suggested by psychotropic treatment trends, receives various care reflecting an individual's cultural context. In the WHO's publication *Caring for children and adolescents with mental disorders* (2003), the poor prognosis of major depressive disorder in young people is mentioned as a cross-cultural concern. The development of paediatric depression has a high rate of continuing mental disorders into adulthood, including the continuation of major depression, bipolar disorder, substance abuse and suicidality, and shows significantly increased rates of hospitalisations and psychosocial impairments, along with lower academic success. While paediatric data is not included, the Jordanova et al. (2010) study in Eastern Europe indicates depression as one of the most common psychiatric diagnoses in that region, and states that 83.4% of depression patients are prescribed antidepressants and 19% receive concomitant prescriptions for two antidepressants. While overall psychotropic treatment in this study was suggested to be outdated and/or prescribed off-label, there is a higher prescription rate for newer antidepressants (46%), while SSRIs and older generations of antidepressants are prescribed at slightly lower rates (29.4% and 29.1% respectively). As noted above, it would be interesting to see if and how these prescription practices are extended to the paediatric population in this region, whether it is common for children and adolescents to be diagnosed with depression and then receive similar antidepressant treatment to adults, as well.

While France is recognised as having one of the highest prescription rates in the world, the prevalence of SSRIs is not as high in the French paediatric population as the prevalence of some other psychotropics (i.e. antipsychotics and benzodiazepines). As

asserted by Acquaviva et al. (2009), both boys and girls below the age of 13 had a 0.15% to 0.25% frequency of SSRI prescriptions in 2004. As mentioned above, this rate increases with age, rising from 0.4% to 1.4% in males aged 14 onwards and reaching 2.2% in females by age 18. Similar age-specific trends are observed in other Western nations by Zito et al. (2008), though the rate in antidepressant prescription increase varied by region: 'In Germany and the Netherlands, 15-19 year olds were over 3 times more likely to utilize antidepressants than 10-14 year olds, whereas in the US the 15-19 year old group use was only 28% higher than in the younger aged group' (p. 4). The overall prevalence of antidepressant prescriptions also varied across the different regions, being more than five times more prevalent in the US than the Netherlands and Germany according to the data presented by Zito et al. (2008), and consistent with previous studies consulted asserting higher rates of US antidepressant use. The class of antidepressants prescribed also differed; TCAs represent the majority of antidepressant prescriptions in Germany, about half the prescriptions in the Netherlands, and only a minority of prescriptions in the US, and the inverse trend is observed for SSRI prevalence. With the changes made to paediatric prescribing policy in the mid-2000s in both the US and EU since this data was collected, it would be interesting to see the effect on prevalence rates, particularly concerning the rates of SSRI prescriptions; however, it may be anticipated that the comparative trends between the different nations would remain consistent (i.e. the US showing the highest rate of antidepressant prescriptions, followed by the Dutch and then the Germans).

6.4 What effect does culture appear to have on treatment? Further, is medicalising normal a Western phenomenon?

Noting that medical practice is considerably culture-dependent, especially in the field of psychiatry, exploring international trends puts western treatment in context. The US in

particular has significantly higher rates of psychotropic use in the paediatric (and adult) population than the rest of the world. While Western Europe has lower rates than the US, this region also has a fairly common practice of medicating children, and prescription rates both in Europe and in other parts of the world have been steadily increasing, as evidenced by the concern in developing policies. From a survey taken from 2000 to 2002, the lowest increase in psychotropic prescription rate was 13% in Germany, while the highest increase was 68% in the UK over those three years (Timimi, 2008). Despite this emerging trend, it may be expected that the US will remain in the forefront of prescription trends due to its ‘individualist and activist therapeutic mentality’ (Zito et al., 2008, p. 2), whereas other cultures have different values which are equally reflected by medical practice. For example, the study of French paediatric prescription use by Acquaviva et al. (2009) described above notes the higher use of antianxiety medication and sleeping aids, versus the neurostimulant and antidepressant trends found in the US, and the associated diagnostic trends mentioned above. These differences cannot be explained by accessibility to healthcare and medication, but are more likely due to culture beliefs. Even in countries with less of a history of medicating in psychiatry, such as those investigated by Jordanova et al. (2010), common prescription trends differed from Western trends. Eastern European practice tends to use older generation drugs; this was found to be in spite of cost efficiency, but may perhaps reflect the level of development of their mental health services in that region. In what was formerly referred to as the ‘Second World’⁴, as well as in other less developed regions, it is possible that the difference in treatment and/or lack of treatment is strongly influenced by limited availability of mental health services and access to those services, but it may also be influenced by different cultural beliefs and social attitudes toward mental health care. Moreover, just as prescribing trends differ due to culture, so too will diagnostic trends, in part

⁴ The Second World refers to the former communist countries of the Soviet Union and Eastern Europe (Giddens, 2006).

due to the use of different diagnostic systems, but also cultural views of particular disorders and the need to treat certain aspects of mental health. This is evidenced, for instance, by the diagnostic tendencies in France noted above, as well as higher diagnosing of psychosis in Eastern Europe (Jordanova et al., 2010).

A closer look at Western paediatric psychiatry by Timimi (2004; 2006; 2008) strengthens the notion that medicalisation is a phenomenon that is characteristic of Western culture. In general, following World War II, the West has tended to promote permissiveness, individualism and the associated rights of children, which is suggested to be a consequence of the collapse of the stable family environment. This trend has resulted in evolving markets targeting the young population as consumers and blurring the distinction between childhood and adulthood. Children develop a value system based the influence of their parents and especially their culture, and ‘in the West children are socialised into a system that embraces a particular idea of freedom through promoting individualism, competitiveness, inequality and the rejection of forms of authority’ (Timimi, 2006, p. 36). Consequently, the Western culture fosters an increase in self-examination and self-awareness, which then endorses medicalisation as individuals identify more of their own inadequacies. Though medicalisation, then, is a product of cultural values, it inherently removes the examination of context, including the broader cultural context that advances it. Further, this emphasis on competition and individualism causes parental and professional anxiety to increase in an effort to promote a child’s achievement of his or her full potential, and such pressures also increase the child’s anxiety and trigger psychopathology (Timimi, 2008). In the case of paediatric depression, as identification of depressed children increases, whether this increase is due to the changing diagnostic criteria or the cultural context is unclear. Timimi (2004) suggests that the greater influence on this increase is the sociocultural changes described above, which cause greater unhappiness during childhood.

Extending this analysis to other countries, Timimi (2006) discusses the imposition the West has made on other countries' cultural beliefs with regard to childrearing and paediatric mental health problems. Many non-Western countries have a very different family-centred culture, where duty and responsibility to the extended family is the primary focus. For instance, the Organization of African Unity has produced a child-protection policy that was structured around family responsibility, not child rights. However, in Asia, Western theories are bleeding into childcare practices, as some Asian experts begin to argue that 'many of the traditional beliefs and practices of Asians prevent them from seeking and using new scientific knowledge in childrearing' (Timimi, 2006, p. 37). Although, why are Western scientific advances assumed to be better? Normality and disorder are functions of culture, so if a culture does not view particular behaviours as problematic, imposing a medicalised view would seem unnecessary, and perhaps even counterproductive as context becomes increasingly discounted. For example, Timimi (2006, 2008) describes a study carried out in 2003 by Brewis and Schmidt in a Mexican school of 200 students, where only one child was diagnosed with ADHD despite 16 children fitting the diagnostic criteria. When discussing the study with parents and teachers at this school, the finding was that ADHD-type behaviours were considered within the realm of normal, age-appropriate behaviours. While Timimi (2006) notes the need to be conscious of context and culturally sensitive to child suffering rather than impressing Western medicalisation on the rest of the world, this view should not discount the attention required by those children who undeniably suffer from mental illness and could benefit from appropriate psychiatric care.

By the evidence provided, it does seem that overall medicalisation is mainly a Western issue, not yet as common in other regions. However, while the West arguably overtreats for mental disorders, countries with less developed mental health services have left

their populations at risk of undertreatment. As Dr. Benedetto Saraceno writes in the Foreword of *Caring for children and adolescents with mental disorders*:

We are well aware of the risks inherent of medicalization in any discussion of mental health problems of children and adolescents – or worse, it's "psychiatrization" – of problems of normal living and normal psychosocial development. We also aware of the many spurious interests endangering an unbiased, objective approach to normal developmental issues, that tend to unduly put many problems of normal living in the basket of "medical or mental disorders".

However, this does not justify a responsible public health officer from shunning action that provides adequate and appropriate interventions for children and adolescents with unequivocal mental disorders. (WHO, 2003, p. 1)

6.5 In summary, what are the ethical implications of treating paediatric depression around the world?

The incorporation of this global perspective infers that paediatric depression is a concern throughout the world. As mentioned above, depression in children and adolescents is noted as a priority disorder by the WHO. Depression in adults is certainly seen everywhere and treated where resources are available; likewise, it can be assumed that young people may have depression independent of where they are in the world, however treatment will be even more limited than that for adults due to minimal availability of appropriate resources (i.e. professionals trained in both mental health care and paediatrics).

There is a spectrum of available mental health services throughout the world, as indicated by the discussion above, which in addition to access to material resources, is also a reflection of cultural values. In the case of depression, consider the presentation of symptoms and criteria for diagnosis. Chapter 1 explained that the DSM and ICD diagnostic systems are culturally sensitive; based on this assumption, does it make sense to fit these two diagnostic systems to various different cultures? This practice would seem equivalent to the difficulty

of applying the adult diagnosis of depression to the atypical presentation found in children. The expression of psychiatric disorder signifies an individual's distress and inability to cope, and understanding of such behaviour is reliant on cultural context. Rather than universally applying the adult diagnosis of depression set out by either the DSM or ICD, it would seem more appropriate to create cultural-specific systems across the world for both adults and children. By sensitizing the diagnosis to the cultural context, global 'depression' will not be addressing exactly the same psychiatric presentation, but it may be a means of identifying and providing appropriate treatment to affected individuals.

CHAPTER 7

What does paediatric depression look like in the clinical setting?: A professional perspective

7.1 Why should practicing clinicians be consulted for this thesis?

Up to this point in the thesis, a critical appraisal of peer-reviewed scientific and clinical literature as well as policy literature has provided a thorough review of relevant information published by researchers, physicians, and policymakers, produced an ethical analysis of this information, and drawn important conclusions concerning the diagnosis and treatment of children and adolescents with mental illness, namely that children are not little adults, diagnosis is subjective, both biology and context must be attended to, and treatment may have different psychological and biological effects in children than in adults. While in published work researchers and clinicians alike may highlight general practice trends and raise specific points of concern or support with regard to the application of psychiatry to the paediatric population, a complete picture of how diagnosis, identity, and treatment fit together in reality is left unclear. By speaking with clinicians directly, the interactive component gained from speaking about the specific issues addressed in this thesis allowed a more thorough analysis of a child's experience of psychiatric disorders, and more specifically depression. Through a focus on depression as well as the use of other anecdotes and years of clinical experience, semi-structured interviews allowed paediatric mental health care specialists to speak directly to those three aspects as related to the care of children and adolescents.

Collecting information through semi-structured interviews is particularly advantageous in the context of this thesis; not only were relevant questions answered, but there was also a discussion element. This method offered an opportunity to gather information and necessary clarification from experts in the field, while also providing these

experts with a fresh perspective on their work. By calling attention to what they automatically do in practice, both the researcher and experts were able to draw novel connections through what has become an instinctive practice for the experts. This new perspective does not *evaluate* the clinicians' work; rather it examines their work from a different viewpoint, focusing on *why* they make certain diagnosis and treatment decisions and how their thinking and practice is determined and reflected by the experiences of the paediatric patients. Also, it is important to note that the practices described in the interviews should not be generalised to be typical national practice, but serve as examples of the way current medical knowledge and guidelines may be applied in a real clinical setting.

7.2 How were the semi-structured interviews carried out?

There were five paediatric clinicians consulted for this thesis, two working for private practices in the US and three working for the NHS in Scotland. The US participants were a doctorate-level general psychologist and a behaviour specialist consultant. The UK participants were two consultant child and adolescent psychiatrists and a third year specialty registrar psychiatrist working with children and adolescents⁵. Ethical approval for this research was granted on 11 March 2011 by the University Teaching and Research Ethics Committee (UTREC) and the Biology School Ethics Committee at the University of St Andrews. The questions guiding the interview are included in Appendix F. Each interview lasted for approximately 15 to 30 minutes, was recorded on a Sony ICD-PX820 Digital Voice Recorder, and deleted following transcription. After the interviews were transcribed, a thematic analysis was carried out on these data to provide comparisons to the broader literature search conducted for this thesis with regard to the purpose of diagnosis, presentation of paediatric depression, common treatments in this population, impact of

⁵ The third year of specialty training in psychiatry is abbreviated as ST3.

disorder, diagnosis and treatment on identity, and the possibility of future neuroenhancement practices in this population. The following codes were applied for referencing purposes: the US psychologist=PC1; the behaviour specialist consultant=PC2; the first UK psychiatric consultant=PC3; the second UK psychiatric consultant=PC4; and the ST3 registrar=PC5. The results are discussed below.

7.3 Based on the professional perspectives given, what is the purpose of diagnosis?

Put simply, diagnosis was described by those interviewed as an identifier. It facilitates developing a treatment plan because it categorises a patient's symptoms and experiences. One of the American clinicians described diagnosis as a means of providing a 'common language of the clinicians,' but also noted that one of the main reasons for providing a diagnosis is because the clinician is expected to do so, 'that's the system' (PC1). As found in the literature search, the American clinicians who were interviewed highlighted the importance of diagnosis as a means of obtaining medical assistance and services, and diagnosis 'starts this machine going' (PC2). The clinical psychologist would determine a diagnosis through a minimum of two 2-hour assessment periods on separate days to take a history, conduct a clinical interview, and gather standardised behavioural reports from parents and teachers. The behavioural specialist does not personally provide a diagnosis, but noted:

Often children are brought in to see a psychiatrist sometimes for 20 minutes to a half hour, [who] listen to the parents' report and, without even having a conversation with the child, develop a diagnosis; they do not do any kind of sustained observation, they aren't getting information from other settings.
(PC2)

This tendency for misdiagnosis may be a result of too much haste to access services and/or medication treatment, as parents come in having read diagnostic criteria on the internet and relate those symptoms they know will grant a necessary, albeit inappropriate, diagnosis.

Likewise, a British psychiatrist noted the inappropriate diagnosis and treatment for paediatric mental disorders as prescribed by general practitioners (GPs) in order to obtain treatment faster, without having to wait to see a specialist (PC3). When patients come to the particular psychiatric clinic in Scotland visited for this thesis however, clinicians tend to avoid giving definitive diagnoses. Except in more severe cases, particularly those with a very clear biological basis determined by a clinical assessment of the history and context of the psychiatric presentation, diagnosis would generally only be given if needed for GP records and is determined using such evaluations as the DSM-IV criteria and Kiddie-SADS semi-structured interview⁶ (PC3) or an ICD checklist and biopsychosocial formulation (described below) (PC4; PC5). For one clinician, the DSM-IV is used as part of the assessment of a patient's condition, but is only one part of a more holistic assessment process, which also integrates assessing the individual's family and school environments (PC3). Based on this practice, a specific diagnosis fails to capture the whole picture. Further, if a diagnostic label is provided, it seems to imply that medication is *the* answer, and that is often not the case (PC3); and particularly for children, who 'mostly are not as resourceful as adults', it is crucial to ensure a strong support system for the patient and address systemic issues in his or her environment, 'e.g. family, school, friends', elements that fall outside a definitive diagnosis (PC4).

The specialty registrar agreed that relying too heavily on diagnosis can be detrimental to the process of receiving appropriate help. While the diagnosis is formed based on a 'constellation of symptoms', the symptoms and the patient get lost behind the label, which medicalises and arguably dehumanises the patients feelings and experiences into a diagnostic code. In this way, if the diagnosis is actually too condensed, then it may be misleading, and 'can result in people really being misunderstood [...] at best and inappropriately managed at

⁶ The Schedule for Affective Disorders and Schizophrenia for School-Age Children (Kiddie-SADS) semi-structured interview is a diagnostic tool used in the paediatric clinical setting to support DSM or ICD diagnosing practices (Lauth et al., 2008).

worst' (PC5). However, the specialty registrar also acknowledged the benefits of giving a diagnosis, which yields to 'guiding treatment, explaining feelings and behaviours, and also [...] accessing support' (PC5). Leading up to whether a particular patient case warrants a diagnosis, the specialty registrar first takes a comprehensive clinical history from the child patient and family, has the patient and family complete a strengths and difficulties questionnaire to measure functioning, and tries to determine the context of the patient's problems in terms of biological, psychological and sociological aetiology (i.e. the biopsychosocial formulation mentioned above). After this analysis, if there is still a suspicion of a particular diagnosis, then typically a structured checklist or score chart is used to match the symptoms with an ICD-10 diagnosis. Though, again, in an aim to treat symptoms, often patients will not necessarily meet strict diagnostic criteria.

While ADHD and depression seem to be the most commonly seen disorders by the clinicians interviewed, there are a number of other patient issues that are typically seen, as well, such as autism, anxiety and anger problems. Also, more recently bipolar disorder in children is becoming more recognised, but because it may present so similarly to other disorders in some cases within this age group, it is very difficult to diagnose in the paediatric population. As one of the British psychiatrists explained, some bipolar patients experience very rapid cycles and are clear cases, but others may more easily get misdiagnosed with ADHD, misconduct, depression, and so on, when there is a more drawn out episodic mood disturbance. Though the novelty of paediatric bipolar disorder sometimes raises concern of overdiagnosis, in actuality misdiagnosis and confusing bipolar with other issues appears to be more common (PC3).

7.4 How does paediatric depression typically present?

While the information gathered in the interviews may not be generalised to the entire population, it may provide an idea of the presentation expected to be seen, particularly in light of the consistency between the interviews, as well as compared to the literature referenced earlier in this thesis. The American clinical psychologist has found that the general symptoms that depressed paediatric patients demonstrate include ‘cutting, lethargy, social withdrawal, really pervasively sad affect, and [...] a lot of anger,’ as well as sleep disorders (PC1). The psychologist also noted that adolescent depression will look different than child depression, and often significant anxiety in children is mistaken for depression and other disorders, including ADHD, misconduct, and even autism. Similar findings were reported by the British clinicians, who listed common symptoms in the paediatric population to include irritability, anxiety, difficulty working, lack of concentration, lack of interest in hobbies, disengagement, social withdrawal (not going out seeing their friends, falling out with friends more, or just not being bothered with them), isolation, self-harm, suicidal thoughts, some sleep disturbance, worrying, very stressed, potential appetite changes, low energy, low mood and unhappiness, negative outlook with regard to oneself and the world, hopelessness and uselessness (PC3; PC4; PC5). Further, a difference based on age was described by one of the British psychiatrists; younger patients will display more angry outbursts and perhaps uncharacteristic difficult behaviour at school, while adolescents show more internalised symptoms and tend to be much better able to explain their symptoms (PC3). Another psychiatrist noted the tendency for girls to more often internalise symptoms than boys (PC4).

7.5 What are the common treatments prescribed for paediatric patients, particularly for depression? And has this been impacted by the changing antidepressant warnings and guidelines over the past six years?

While neither of the American clinicians interviewed can prescribe medications, both were able to comment on the medication use by their clients. As mentioned by the behavioural specialist, children on the autism spectrum are much more commonly treated with psychotropic medication than children in the rest of the population; she estimated that more than 75% of her clients were on some form of psychotropic medication, and several of these children were on four different medications at the same time. The most common medications used by patients coming to that clinic include Ritalin (methylphenidate), Abilify (aripiprazole), Tenex (guanfacine), Strattera (atomoxetine), Vyvance (lisdexamfetamine), and clonidine (PC2). Autism spectrum disorders and associated treatments present a number of concerns, in addition to those discussed regarding child mental health, that will not be addressed in this thesis, but have been investigated elsewhere (e.g. Gerhardt et al., 1991; Elder, 1996; Fuentes & Martin-Arribas, 2007).

The clinical psychologist estimated that about a third of his patients were prescribed psychotropic medication in conjunction with his psychotherapy services, and since he was consulted in order to provide the initial diagnosis, this number would go up to about half of his patients receiving medication at some point in their treatment, particularly for ADHD-stimulant treatment. While significantly less common than stimulants, antidepressants were noted as the second most prevalent drug treatment in the young population seen, and although rarely used in his clientele, the third most notable medication group was that of antipsychotics. Specifically, the antidepressants most commonly prescribed were said to be Prozac (fluoxetine), Lexipro (escitalopram), and Zoloft (sertraline). Often times the patients coming to see the clinical psychologist are medicated by their primary care physician, who

would ask the psychologist for treatment recommendations; the psychologist tends to recommend Prozac first, in part because it is reasonable and prudent to ‘hide a little bit behind what’s approved at what age’ but also because Prozac shows less withdrawal symptoms and lack of serotonin syndrome⁷ if children forget to take a dose of their medication (PC1). After the FDA Black Box Warning was issued, which ‘started because of Paxil (paroxetine) with some children in Canada that weren’t supervised’, prescribing patterns have not seen noticeable changes in his experience; there is simply more concern regarding the monitoring and supervision of children taking antidepressants (PC1). Despite the observation that many parents do not want to bother with the behavioural work and assume the medication will ‘take care of it’, it is very rare that a child on antidepressants will not also be in therapy.

The interviews with British psychiatrists suggested that treatment practices in the UK are comparable to those found in the US. One psychiatrist estimated that up to a third of her patients were taking psychotropic medication (PC3), while the specialty registrar noted that less than 10% of the patients on his caseload were on medication (PC5). Mainly stimulants and antidepressants are the most prevalent in this population, with the rare prescription for antipsychotics. When treating ADHD, the prescriptions are typically for stimulants (e.g. methylphenidate) or atomoxetine, which is a selective norepinephrine reuptake inhibitor (NRI) (PC3; PC4); generally, though, it is more common for GPs to manage ADHD (PC5). In addition to psychotherapy, treatment of severe OCD might call for an SSRI, such as fluoxetine or sertraline. For psychotic illness or more aggressive behaviours accompanying autism, antipsychotics would be prescribed, such as the atypical antipsychotic risperidone or quetiapine. For the treatment of depression in children, following first-line CBT and other psychotherapy, fluoxetine tends to be the first antidepressant prescribed. If fluoxetine

⁷ Serotonin syndrome is an adverse effect to drugs which increase the level of serotonin in the brain, and may be a life threatening reaction (NCBI, 2010).

appeared ineffective, a reassessment of the patient and further family therapy or CBT might be employed, or the prescription of sertraline as a second-line alternative antidepressant if side effects had been an issue with fluoxetine. Both psychiatrists PC3 and PC4 commented on the huge impact the changing guidelines have had on prescription practices, putting fluoxetine at the forefront if medication is the necessary treatment, yet also noted concern with the tendency of GPs to prescribe other treatments despite the guidelines. For instance, one psychiatrist mentioned a specific case of a patient with clear depressive symptoms who was coming in to the psychiatric clinic for an urgent referral due to mismanagement of a citalopram prescription by the GP (PC3).

Also as a result of the changing guidelines and black box warning, the specialty registrar pointed out the benefits of this publicity. The attention given to SSRI use in children and adolescents and the associated increased suicidality has helped raise awareness of antidepressant drug effects in the young population. It has also stimulated finding alternative treatments for paediatric depression other than medication. Alternatives include psychological treatments, such as CBT, interpersonal therapy or psychodynamic-focused therapy exploring past experiences and trauma, and social treatments, such as raising awareness in other people, education, encouraging patients to go out more, helping to plan their day or seeking support from someone willing to go out for lunch or other activities once or twice a week with the patient. If these alternative treatments, particularly talking therapy, are able to help increase motivation, then often the need for (potentially harmful) medication may be negated (PC5).

7.6 What impact does the experience of a mental disorder, diagnosis, and treatment appear to have on identity development?

Before discussing identity explicitly, apparent self-awareness in paediatric patients was addressed in the interviews. Generalised from all the interviews, while perhaps a function of the patient's age or severity of disorder, often patients are aware that there is a problem, and thus, are aware of why they are seeing a mental health specialist. Many paediatric patients, particularly those in adolescence, can recognise their own distress. That being said, despite this awareness, children and adolescents are not the ones who decide whether or not they should see a specialist, rather it is decided by their parents. As the American psychologist stated, 'We don't see kids because they want to be seen, we see them because the adults want them to be seen. That's an essential difference between working with children and working with adults' (PC1).

Whether paediatric patients are aware of their disorder or not, their experiences resulting from the disorder, diagnosis, and/or treatment may certainly affect their sense of who they are and how they view themselves as they continue to develop an identity as individuals. Though medicalising experience by providing a diagnostic label is arguably forcing an internalization of the disorder, it may also remove a sense of self-blame and yield relief for some. The American psychologist suggested that children may be more upset by a lack of diagnosis due to the 'impact that they're less capable and the negative judgemental quality of the interactions' experienced by disordered individuals; therefore, a diagnosis in such cases would mean that the individual may not feel at fault for these negative experiences, and in fact, there may be hope for improvement through treatment (PC1).

On the other hand, use of the diagnostic label may be considered less helpful for some patients. As described above, the British clinicians interviewed suggested avoiding definitive diagnostic labels in order to take the focus away from solely biological causes and/or

medication treatments. There are some patients who may clearly show a more isolated biological (versus psychological) illness, which appears to interrupt normal premorbid functioning and identity development; for example, if a previously normally developing child becomes depressed, that child may experience a disturbance in his or her sense of identity and/or daily functioning due to the depressive process. In such a case, diagnosing, explaining and treating the disorder effectively makes the child better and is the straightforward path toward the child 'getting back on track' (PC3).

Though, getting better in chronic cases may not be as simple; in addition to experiencing the disorder itself, these patients may have been subject to bullying at school or family difficulties, issues which definitely affect the child's development of identity and should be dealt with through CBT and family therapy sessions. The specialty registrar gave an example of a 14 year old girl with ADHD whom he had on his caseload, who despite the usefulness of stimulant medication to resolve some issues, the disorder itself included relationship problems between the patient and her mother and teachers, for example, which could not simply be taken care of by medication. The patient required more extensive psychotherapy and support because the ADHD impacted her identity in more ways than a tablet could resolve by only addressing biology (PC5). For young patients who are already struggling with their identity, giving such a specific diagnostic label only addresses part of the problem. Thus, it is even more important that paediatric patients receive CBT as part of their treatment, which would address self-esteem and the way the patient views the world, giving the disorder personal context. Particularly for younger patients, they may feel very little sense of autonomy, whereas older adolescent patients may feel more in control of themselves, but in either case psychotherapy could speak to this issue. Through family sessions, pathology and normal adolescent behaviour can become more distinguishable, which may lead to a greater ability to trust the young patient and help him or her develop a

stronger sense of autonomy and responsibility for their actions (PC3). However, in some cases, as discussed by the specialty registrar, the stigma associated with treatment regardless of the form, may negatively impact identity development as well. Having to explain that he or she needs to see a psychiatrist or take medication can cause so much additional stress that psychiatric treatment is stopped, even if the patient was initially open to CBT, medication, and/or other psychiatric treatment (PC5).

7.7 Is there a future for neuroenhancement in the paediatric population?

The practice of paediatric neuroenhancement continues to be considerably controversial. In light of the antidepressant enhancement trend in adults (e.g. as discussed by Degrazia, 2000; Elliott, 2004; Parens, 2004) and the increasing neurostimulant enhancement trend in children (e.g. as discussed by Singh, 2008; Singh & Kelleher, 2010; Parens & Johnston, 2011), this topic was discussed briefly during the interviews with clinicians. All five clinicians interviewed voiced opposition to the use of medication for enhancement purposes. The American psychologist would discourage neurostimulant use unless absolutely necessary for treatment of a disorder ‘because it’s not a cure and we’re also looking at duration’. In this context, duration is referring to the length of time one dose remains effective; the example given was Strattera, which lasts for 24 hours, making it less prone to the misuse and abuse by university students, for instance. He also noted, however, the importance of psychotropic drugs as a valuable and effective tool if used selectively and properly for those requiring treatment of a disorder.

Due to the effectiveness of newer psychotropic drugs in general, not only neurostimulants, the grey area between treatment and enhancement in paediatric psychiatry increases, in terms of depression as well as other disorders; if not treating a distinct disorder or dysfunction, then ‘treatment’ may edge toward ‘enhancement’, as discussed earlier in this

thesis. One of the British psychiatrists commented on the difficulty of making the decision to medicate in such borderline cases. The thought process in such cases might be, ‘Well, they don’t quite fit the criteria, but they really want [medication]. Maybe that’s the way to get them engaged, and they are going to come and talk to me, as well; ok, we’ll go for it, [...] in general, it’s not particularly harmful as long as you follow them up. [...] We’re very clear about what we’re expecting to see from this and what you can’t expect to see’ (PC3). Some patients show improvements and others do not; and whether improvements might just be placebo effects is also unclear. However, in terms of a patient desiring medication specifically for the purpose of enhancement, one of the psychiatrists stated, ‘I can see why people might want to do that and maybe perform better in exam situations but think it gives a person a better sense of self worth and achievement if they feel they did it themselves’ (PC4).

On the other hand, as the specialty registrar pointed out, it is very common to take stimulants, such as coffee or Red Bull, or other enhancers, such as omega-3 fish oils, so enhancement itself is already being practised. Although, when introducing prescription drugs into the enhancement context, the debate over who gets treatment and who does not becomes an issue, and may presumably be even more problematic for the NHS if it supports non-essential medicine. Further, the risks of taking drugs such as SSRIs for enhancement purposes may be fairly dangerous as the drugs are not without side effects, including ‘GI disturbances, [...] increased agitation, [...] increased suicidality, [...] precipitating hypomania or mania’, and certainly might not outweigh the benefits of enhancement; whereas, the benefit of relieving impairment could more realistically outweigh those same risks (PC5). The specialty registrar went on to say that many people have maladaptive personality traits and stress may cause some level dysfunction (e.g. getting angry when hungry), and giving someone Prozac, for instance, might help manage these traits; however, as mentioned by the clinical psychologist, this is not curing the cause of the problem, which may be better

addressed by psychotherapy instead. The difficulty with counselling as an alternative enhancement is partially access, public acceptance, and the inconvenience as compared to just taking a tablet. Then the issue of medicalisation arises; giving a diagnosis and focusing on the *biological* treatment through medication can help some people, but should this be the practice for treating and essentially enhancing ‘normal’ people who are more likely experiencing *psychological* problems? According to the clinicians interviewed for this thesis, the latter psychological issues faced by normal people may be better treated through CBT and other methods addressing contextual problems faced by the individual, rather than medicating non-disordered children and adolescents.

7.8 In summary, did the information conveyed by practicing clinicians reflect what was found in the literature?

Overall, the interviews with clinicians were consistent with information found in the literature. Furthermore, the various clinicians often reflected similar information pertaining to the use of diagnosis, presentation of paediatric depression, psychiatric treatment in the paediatric population, the effect of psychiatric experience on identity development, and paediatric neuroenhancement, regardless of specific profession or location of practice. In certain cases, a diagnosis was found to be very helpful in order to best explain a patient’s experiences and feelings as well as direct treatment, but the clinicians also specified that it should be applied with careful consideration due to the tendency to discount a patient’s context when there is a specific diagnosis given. Though every case of depression has a unique presentation, there are a number of very common symptoms listed by the different clinicians, generally shifting from externalising behaviours towards internalising symptoms as a function of age. Both in the US and UK, prescribing practices outlined by the literature and interviews tend to concern mainly stimulants and antidepressants, and SSRI prescriptions

are most often for fluoxetine, as suggested by UK guidance and the FDA black box warning. Further, the clinicians interviewed commented that there is typically a noticeable negative effect on identity development caused by experiencing a psychiatric disorder during childhood and adolescence, which is often, but not always, improved through appropriate treatment. While all the clinicians initially rejected the practice of neuroenhancement, particularly in children, they also acknowledged the possibility of an increasing trend in enhancement. Although psychotropic medications have become a very valuable clinical tool, serious risks remain associated with use in the paediatric population, whether for treatment or enhancement purposes, and thus, should be used with caution.

Chapter 8

Conclusion

This thesis has investigated the key ethical concerns involved in the diagnosis and treatment of paediatric mental health disorders, and specifically examined these concerns within the context of paediatric depression. By addressing these issues through the lens of depression, the experience of disordered children and adolescents highlights the relevant ethical considerations, and may serve as ethical guidance in the treatment of paediatric mental health care. Specifically, ethical guidance refers to the standard points involving moral judgements that must be taken into account by both the clinician and patient (including parents) in order to most benefit child and adolescent psychiatric patients. While this thesis explores the ethical issues from the historical, philosophical, psychological, biological, cultural, and professional perspectives individually, many of the points raised are not confined to one perspective, nor are they entirely independent from one another. There are thirteen major ethical concerns to be considered when diagnosing and treating children for mental health disorders, which may be grouped into three parts: identity development and paediatric physiology within developmental issues; subjectivity of diagnosis, accuracy and appropriateness of diagnosis, medicalisation and prevalence of disorder within diagnostic issues; and consent and confidentiality, access to services, paradox of psychotropic use in paediatrics, lack of treatment data, inability to directly apply adult data to paediatrics, treatment paradox with normal individuals and linking neurobiology to psychology within treatment issues.

Due to their stage of development, children and adolescents cannot be considered as simply little adults. Firstly, in terms of psychology, paediatric patients are in the process of *developing their identity*. Based on the findings in this thesis, by giving a diagnosis and/or providing treatment, these labels and experiences often appear to be integrated into the young

patients' understanding of themselves, leaving a lasting imprint on their concept of self more so than if they had already held a matured understanding of self. This psychological sensitivity relates to the issues of diagnosis discussed below. Secondly, children and adolescents are *physiologically different than adults*, and within the context of psychiatry, the plasticity of the immature brain leaves young patients particularly vulnerable to the development of psychopathology as well as to the effects of psychotropic treatment. Physiological immaturity relates to the treatment issues discussed below.

Within the area of diagnosis itself, there are four elements. Firstly, the *subjectivity of a diagnosis* requires consideration, particularly in borderline cases. While diagnosis is based on an arbitrary distinction, as determined by a discrete number of symptoms and/or a clinician's professional judgment, it is associated with both benefits and detriments; therefore, the lack of an absolute definition brings up the second diagnostic issue, that of *accuracy and appropriateness*. A diagnosis rarely provides a perfect definition of a patient's problems, and though the diagnosis typically directs an appropriate treatment plan, if the diagnosis is not accurate, the treatment associated with the given diagnosis can have negative effects, such as unnecessary and inappropriate prescriptions, added stress or inadequate support services. Thirdly, the issue of *medicalisation* when treating the paediatric population requires additional attention for two reasons: its tendency to discount context and its implications for the future of both the patients themselves as well as society as a whole. With respect to context, this is a crucial factor of any psychiatric disorder, for which diagnoses are made based on impaired functioning within an individual's environment. Thus, removing context from the equation that formulates a treatment plan seems contradictory; although medicalising problems may improve a patient's condition to some extent, it has the tendency to yield a biological and medication-orientated focus which cannot fully dissolve psychiatric problems. In terms of the future implications of medicalisation practices, this runs the risk of

subjecting young patients to treatments that will affect both their psychological and physiological development, as discussed above, and ultimately questions our society's definition of normal and what is expected behaviour and functioning. This relates to the fourth and final diagnostic issue, which is the true *prevalence of psychiatric disorders* in children across the world. While psychiatric disorders have been found to exist worldwide, the definition of 'normal' behaviour versus diagnosable pathology is subjective by nature, as mentioned above. Medicalisation is considered a Western issue, but is bleeding into psychiatric practices everywhere, again narrowing focus farther away from a patient's context, which is in fact a crucial element of psychiatric problems and treatments.

As stated above, paediatric patients are not little adult patients, and cannot be treated as such. Treatment issues may be described in seven parts, which are all intertwined. Firstly, the process of treating paediatric patients is complicated by different *consent and confidentiality* practices than those for adults. While children may provide assent for treatment, consent is granted by adults; therefore, treatment will always be out of the child's control to some degree and requires adults in order to access care. Further, confidentiality between the clinician and child patient is muddled by the inclusion of parents or other adults required for treatment consent. The second issue in paediatric treatment is physical *access to services*. Appropriate treatments are made available by adults, whether it be the parent/guardian decision to seek services or the presence of resources in the region, both of which are guided by environmental context. The third treatment issue is the *paradox of psychotropic use* in the paediatric population; the paradox is a result of the risk of treating children with drugs lacking appropriate data countered by the difficulty of conducting research in paediatrics, a vulnerable population. Fourthly, the *lack of treatment data* in the paediatric population is an issue in itself. The practice of treating adults off-label is generally avoided and potentially dangerous; this should also be the case for treating children, and the

only way to remedy the issue is to conduct the required research of treatment effects. This feeds into the issue of *extending adult data* to paediatric practice; due to physiological differences both the short and long term effects of drugs are different in children than adults, so adult data cannot simply replace paediatric-specific studies. The sixth issue concerns a further *complication of the paediatric treatment paradox* when prescribing medications for arguably ‘normal’ individuals, because not only do psychotropic effects differ between adults and children, but also between pathological and normal individuals. Again, it is even more ethically challenging to conduct research on treatment effects in ‘normal’ children than in disordered children due to the lack of dysfunction and impairment. Lastly, particularly when providing treatment for enhancement purposes, the *effects that biological changes will have on psychology* must be considered. Neurophysiology and cognition should both be included in clinical assessments, both through the treatment of psychotherapy and medication, because they are so closely linked, as suggested for instance by the effect psychological stress has on neurochemical levels and the effect of psychotropic medications on cognitive style.

While all of these issues have been identified in the available literature, they have previously been presented with regard to a specific perspective, i.e. biology, psychology, culture, etc. However, as the ethical issues are drawn together in this thesis, it becomes clear that the different disciplines are actually raising many similar and/or related concerns, which cannot be isolated from one another. The shared interface between the different perspectives should not be overlooked, as the various angles share the same objective of raising awareness and improving treatment of paediatric mental health care. With the added perspective provided by professional interviews focused to the context of this thesis, the interdisciplinary application within the clinical setting of the various ethical concerns highlights the importance of recognising the overlap of disciplines as it appears in actual care practices,

particularly considering the consistency of results across the different professions within paediatric mental health care, a comparison not found in the literature.

The strengths of this thesis include its scope of the various disciplines, interplay between generalised and disorder-specific application of the ethical concerns and inclusion of both literature and interpersonal data. Exploring the ethical arguments presented by different disciplines regarding the same topic, paediatric mental health care, allows a unique interdisciplinary perspective to develop. Further, by incorporating both general paediatric mental health care as well as information specific to depression, the thirteen points outlined above provide ethical guidance applicable to the entire field of paediatric psychiatry through the example of paediatric depression; it demonstrates how general issues may apply to a particular diagnosis as well as how concerns raised in the treatment of depression may be extended to a broader context. Additionally, the interviews followed the literature-based section, in order to tie together the wide scope of disciplines in the way that appears in real practice, an element that becomes lost in literature focused on specific aspects of care.

Weaknesses of this thesis include the limited sample size of clinicians interviewed and the inability to include data collected directly from paediatric patients. Due to the small number of clinicians included in the data set, results are very specific, both in terms of profession of individuals interviewed and the location of their clinical practices, and thus, may not be extended to typical national practice trends. Not including primary data from children and adolescents requires that paediatric experiences are based only on the relaying of information from the literature and clinicians, which risks the accuracy of portraying a child or adolescent's true experience. While the constraints of this thesis did not allow for the collection of such data, other similar studies which do include a more extensive data set are in progress. Currently, the Voices On Identity, Childhood, Ethics and Stimulants (VOICES) project by Dr. Ilina Singh and colleagues addresses many of the issues noted in this thesis

within the context of ADHD through a collection of interviews conducted between 2008 to 2010 with children ages 9-14 in the US and UK, investigating the impact of disorder, diagnosis and treatment on paediatric patients from the children's perspective (VOICES, 2008); the results of this study are still in the process of being analysed, but once completed will provide a very interesting parallel to the conclusions drawn in this thesis.

Overall, this thesis provides a framework for future investigation of the ethics of diagnosing and treating paediatric mental health disorders by drawing together an interdisciplinary overview of the ethical concerns and how those concerns ought to be considered and applied relative to a specific disorder. Despite the limited data available at present, an ever-increasing number of children are being treated. As these trends continue, research should address the longitudinal impact increased paediatric treatment will have on the future of these individuals—what is the prognosis for today's young patients? Also, how will medicalisation shape the future of society? Since medicalisation, diagnosis and treatment decisions are subjective, further studies regarding the factors determining these judgments may look into the interplay of clinician opinion, media influence, and individual patients' access to information. With the first generation of more medicalised and heavily treated children entering adulthood, the implications of earlier treatment trends are beginning to surface on a broader cultural scale that cannot be overlooked.

Appendix A

ICD 10 Diagnosis of Depression

(Sections F33 and F32)

As found in:

Internet Mental Health, 2009. *Major Depressive Disorder*. [online] Available at:
<<http://www.mentalhealth.com/icd/p22-md01.html>> [Accessed: 3 June 2011].

F33 Recurrent Depressive Disorder

The disorder is characterized by repeated episodes of depression as specified in depressive episode (mild, moderate, or severe), without any history of independent episodes of mood elevation and overactivity that fulfill the criteria of mania. However, the category should still be used if there is evidence of brief episodes of mild mood elevation and overactivity which fulfill the criteria of hypomania immediately after a depressive episode (sometimes apparently precipitated by treatment of a depression). The age of onset and the severity, duration, and frequency of the episodes of depression are all highly variable. In general, the first episode occurs later than in bipolar disorder, with a mean age of onset in the fifth decade. Individual episodes also last between 3 and 12 months (median duration about 6 months) but recur less frequently. Recovery is usually complete between episodes, but a minority of patients may develop a persistent depression, mainly in old age (for which this category should still be used). Individual episodes of any severity are often precipitated by stressful life events; in many cultures, both individual episodes and persistent depression are twice as common in women as in men.

The risk that a patient with recurrent depressive disorder will have an episode of mania never disappears completely, however many depressive episodes he or she has experienced. If a manic episode does occur, the diagnosis should change to bipolar affective disorder.

Recurrent depressive episode may be subdivided, as below, by specifying first the type of the current episode and then (if sufficient information is available) the type that predominates in all the episodes.

Includes:

- * recurrent episodes of depressive reaction, psychogenic depression, reactive depression, seasonal affective disorder
- * recurrent episodes of endogenous depression, major depression, manic depressive psychosis (depressed type), psychogenic or reactive depressive psychosis, psychotic depression, vital depression

Excludes:

- * recurrent brief depressive episodes

F32 Depressive Episode

In typical depressive episodes of all three varieties described below (mild, moderate, and severe), the individual usually suffers from depressed mood, loss of interest and enjoyment, and reduced energy leading to increased fatigability and diminished activity. Marked tiredness after only slight effort is common. Other common symptoms are:

- (a) reduced concentration and attention;
- (b) reduced self-esteem and self-confidence;
- (c) ideas of guilt and unworthiness (even in a mild type of episode);
- (d) bleak and pessimistic views of the future;
- (e) ideas or acts of self-harm or suicide;
- (f) disturbed sleep;
- (g) diminished appetite.

The lowered mood varies little from day to day, and is often unresponsive to circumstances, yet may show a characteristic diurnal variation as the day goes on. As with manic episodes, the clinical presentation shows marked individual variations, and atypical presentations are particularly common in adolescence. In some cases, anxiety, distress, and motor agitation may be more prominent at times than the depression, and the mood change may also be masked by added features such as irritability, excessive consumption of alcohol, histrionic behaviour, and exacerbation of pre-existing phobic or obsessional symptoms, or by hypochondriacal preoccupations. For depressive episodes of all three grades of severity, a duration of at least 2 weeks is usually required for diagnosis, but shorter periods may be reasonable if symptoms are unusually severe and of rapid onset.

Some of the above symptoms may be marked and develop characteristic features that are widely regarded as having special clinical significance. The most typical examples of these "somatic" symptoms are: loss of interest or pleasure in activities that are normally enjoyable; lack of emotional reactivity to normally pleasurable surroundings and events; waking in the morning 2 hours or more before the usual time; depression worse in the morning; objective evidence of definite psychomotor retardation or agitation (remarked on or reported by other people); marked loss of appetite; weight loss (often defined as 5% or more of body weight in the past month); marked loss of libido. Usually, this somatic syndrome is not regarded as present unless about four of these symptoms are definitely present.

The categories of mild, moderate and severe depressive episodes described in more detail below should be used only for a single (first) depressive episode. Further depressive episodes should be classified under one of the subdivisions of recurrent depressive disorder.

These grades of severity are specified to cover a wide range of clinical states that are encountered in different types of psychiatric practice. Individuals with mild depressive episodes are common in primary care and general medical settings, whereas psychiatric inpatient units deal largely with patients suffering from the severe grades.

Acts of self-harm associated with mood (affective) disorders, most commonly self-poisoning by prescribed medication, should be recorded by means of an additional code from Chapter XX of ICD-10 (X60-X84). These codes do not involve differentiation between attempted suicide and "parasuicide", since both are included in the general category of self-harm.

Differentiation between mild, moderate, and severe depressive episodes rests upon a complicated clinical judgement that involves the number, type, and severity of symptoms present. The extent of ordinary social and work activities is often a useful general guide to the likely degree of severity of the episode, but individual, social, and cultural influences that disrupt a smooth relationship between severity of symptoms and social performance are sufficiently common and powerful to make it unwise to include social performance amongst the essential criteria of severity.

The presence of dementia or mental retardation does not rule out the diagnosis of a treatable depressive episode, but communication difficulties are likely to make it necessary to rely more than usual for the diagnosis upon objectively observed somatic symptoms, such as psychomotor retardation, loss of appetite and weight, and sleep disturbance.

Includes:

* single episodes of depression (without psychotic symptoms), psychogenic depression or reactive depression)

F32.0 Mild Depressive Episode

Diagnostic Guidelines:

Depressed mood, loss of interest and enjoyment, and increased fatigability are usually regarded as the most typical symptoms of depression, and at least two of these, plus at least two of the other symptoms described above should usually be present for a definite diagnosis. None of the symptoms should be present to an intense degree. Minimum duration of the whole episode is about 2 weeks.

An individual with a mild depressive episode is usually distressed by the symptoms and has some difficulty in continuing with ordinary work and social activities, but will probably not cease to function completely.

A fifth character may be used to specify the presence of the somatic syndrome:

F32.00 Without somatic symptoms

The criteria for mild depressive episode are fulfilled, and there are few or none of the somatic symptoms present.

F32.01 With somatic symptoms

The criteria for mild depressive episode are fulfilled, and four or more of the somatic symptoms are also present. (If only two or three somatic symptoms are present but they are unusually severe, use of this category may be justified.)

F32.1 Moderate Depressive Episode

Diagnostic Guidelines:

At least two of the three most typical symptoms noted for mild depressive episode should be present, plus at least three (and preferably four) of the other symptoms. Several symptoms are likely to be present to a marked degree, but this is not essential if a particularly wide variety of symptoms is present overall. Minimum duration of the whole episode is about 2 weeks.

An individual with a moderately severe depressive episode will usually have considerable difficulty in continuing with social, work or domestic activities.

A fifth character may be used to specify the occurrence of somatic symptoms:

F32.10 Without somatic symptoms

The criteria for moderate depressive episode are fulfilled, and few if any of the somatic symptoms are present.

F32.11 With somatic symptoms

The criteria for moderate depressive episode are fulfilled, and four or more of the somatic symptoms are present. (If only two or three somatic symptoms are present but they are unusually severe, use of this category may be justified.)

F32.2 Severe Depressive Episode Without Psychotic Symptoms

In a severe depressive episode, the sufferer usually shows considerable distress or agitation, unless retardation is a marked feature. Loss of self-esteem or feelings of uselessness or guilt are likely to be prominent, and suicide is a distinct danger in particularly severe cases. It is presumed here that the somatic syndrome will almost always be present in a severe depressive episode.

Diagnostic Guidelines:

All three of the typical symptoms noted for mild and moderate depressive episodes should be present, plus at least four other symptoms, some of which should be of severe intensity. However, if important symptoms such as agitation or retardation are marked, the patient may be unwilling or unable to describe many symptoms in detail. An overall grading of severe episode may still be justified in such instances. The depressive episode should usually last at least 2 weeks, but if the symptoms are particularly severe and of very rapid onset, it may be justified to make this diagnosis after less than 2 weeks.

During a severe depressive episode it is very unlikely that the sufferer will be able to continue with social, work, or domestic activities, except to a very limited extent.

This category should be used only for single episodes of severe depression without psychotic symptoms; for further episodes, a subcategory of recurrent depressive disorder should be used.

Includes:

- * single episodes of agitated depression
- * melancholia or vital depression without psychotic symptoms

F32.3 Severe Depressive Episode With Psychotic Symptoms

Diagnostic Guidelines:

A severe depressive episode which meets the criteria given for severe depressive episode without psychotic symptoms and in which delusions, hallucinations, or depressive stupor are present. The delusions usually involve ideas of sin, poverty, or imminent disasters, responsibility for which may be assumed by the patient. Auditory or olfactory hallucinations are usually of defamatory or accusatory voices or of rotting filth or decomposing flesh.

Severe psychomotor retardation may progress to stupor. If required, delusions or hallucinations may be specified as mood-congruent or mood-incongruent.

Differential

Diagnosis:

Depressive stupor must be differentiated from catatonic schizophrenia, from dissociative stupor, and from organic forms of stupor. This category should be used only for single episodes of severe depression with psychotic symptoms; for further episodes a subcategory of recurrent depressive disorder should be used.

Includes:

- * single episodes of major depression with psychotic symptoms, psychotic depression, psychogenic depressive psychosis, reactive depressive psychosis

Appendix B

DSM IV Diagnosis of Depression

As found in:

Depression Today, 2010. *DSM IV Criteria*. [online] Available at: < <http://www.mental-health-today.com/dep/dsm.htm> > [Accessed: 3 June 2011].

Major Depressive Episode

A. Five (or more) of the following symptoms have been present during the same 2-week period and represent a change from previous functioning; at least one of the symptoms is either (1) depressed mood or (2) loss of interest or pleasure.

Note: Do not include symptoms that are clearly due to a general medical condition, or mood-incongruent delusions or hallucinations.

(1) Depressed mood most of the day, nearly every day, as indicated by either subjective report (e.g., feels sad or empty) or observation made by others (e.g., appears tearful). **Note:** In children and adolescents, can be irritable mood.

(2) Markedly diminished interest or pleasure in all, or almost all, activities most of the day, nearly every day (as indicated by either subjective account or observation made by others).

(3) Significant weight loss when not dieting or weight gain (e.g., a change of more than 5% of body weight in a month), or decrease or increase in appetite nearly every day. **Note:** In children, consider failure to make expected weight gains.

(4) Insomnia or hypersomnia nearly every day.

(5) Psychomotor agitation or retardation nearly every day (observable by others, not merely subjective feelings of restlessness or being slowed down).

(6) Fatigue or loss of energy nearly every day.

(7) Feelings of worthlessness or excessive or inappropriate guilt (which may be delusional) nearly every day (not merely self-reproach or guilt about being sick).

(8) Diminished ability to think or concentrate, or indecisiveness, nearly every day (either by subjective account or as observed by others).

(9) Recurrent thoughts of death (not just fear of dying), recurrent suicidal ideation without a specific plan, or a suicide attempt or a specific plan for committing suicide.

B. The symptoms do not meet criteria for a Mixed Episode.

C. The symptoms cause clinically significant distress or impairment in social, occupational, or other important areas of functioning.

D. The symptoms are not due to the direct physiological effects of a substance (e.g., a drug of abuse, a medication) or a general medical condition (e.g., hypothyroidism).

E. The symptoms are not better accounted for by Bereavement, i.e., after the loss of a loved one, the symptoms persist for longer than 2 months or are characterized by marked functional impairment, morbid preoccupation with worthlessness, suicidal ideation, psychotic symptoms or psychomotor retardation.

Major Depressive Disorder

Single Episode:

- A. Presence of a single Major Depressive Episode.
- B. The Major Depressive Episode is not better accounted for by Schizoaffective Disorder and is not superimposed on Schizophrenia, Schizophreniform Disorder, Delusional Disorder, or Psychotic Disorder Not Otherwise Specified.
- C. There has never been a Manic Episode, a Mixed Episode, or a Hypomanic Episode.
Note: This exclusion does not apply if all the manic-like, mixed-like, or hypomanic-like episodes are substance or treatment induced or are due to the direct physiological effects of a general medical condition.

Recurrent:

- A. Presence of two or more Major Depressive Episodes.
Note: To be considered separate episodes, there must be an interval of at least 2 consecutive months in which criteria are not met for a Major Depressive Episode.
- B. The Major Depressive Episodes are not better accounted for by Schizoaffective Disorder and are not superimposed on Schizophrenia, Schizophreniform Disorder, Delusional Disorder, or Psychotic Disorder Not Otherwise Specified.
- C. There has never been a Manic Episode, a Mixed Episode, or a Hypomanic Episode.
Note: This exclusion does not apply if all the manic-like, mixed-like, or hypomanic-like episodes are substance or treatment induced or are due to the direct physiological effects of a general medical condition.

Specify (for current or most recent episode):

Severity/Psychotic/Remission Specifiers

Chronic

With Catatonic Features

With Atypical Features

With Postpartum Onset

Specify

Longitudinal Course Specifiers (With and Without Interepisode Recovery)

With Seasonal pattern

Appendix C

List of Antidepressant Drugs Requiring FDA Medication Guides

As found in:

FDA, 2010b. *Antidepressant Use in Children, Adolescents, and Adults*. [online] (Updated: 12 August 2010) Available at: <<http://www.fda.gov/Drugs/DrugSafety/InformationbyDrugClass/ucm096273.htm>> [Accessed: 11 June 2011].

- Anafranil (clomipramine)
- Asendin (amoxapine)
- Aventyl (nortriptyline)
- Celexa (citalopram hydrobromide)
- Cymbalta (duloxetine)
- Desyrel (trazodone HCl)
- Elavil (amitriptyline)
- Effexor (venlafaxine HCl)
- Emsam (selegiline)
- Etrafon (perphenazine/amitriptyline)
- fluvoxamine maleate
- Lexapro (escitalopram oxalate)
- Limbitrol
(chlordiazepoxide/amitriptyline)
- Ludiomil (maprotiline)
- Marplan (isocarboxazid)
- Nardil (phenelzine sulfate)
- nefazodone HCl
- Norpramin (desipramine HCl)
- Pamelor (nortriptyline)
- Parnate (tranylcypromine sulfate)
- Paxil (paroxetine HCl)
- Pexeva (paroxetine mesylate)
- Prozac (fluoxetine HCl)
- Remeron (mirtazapine)
- Sarafem (fluoxetine HCl)
- Seroquel (quetiapine)
- Sinequan (doxepin)
- Surmontil (trimipramine)
- Symbyax (olanzapine/fluoxetine)
- Tofranil (imipramine)
- Tofranil-PM (imipramine pamoate)
- Triavil (perphenazine/amitriptyline)
- Vivactil (protriptyline)
- Wellbutrin (bupropion HCl)
- Zoloft (sertraline HCl)
- Zyban (bupropion HCl)

Appendix D

Revisions to FDA Black Box Product Labeling

As found in:

FDA, 2010c. *Revisions to Product Labeling*. [online] Available at: <<http://www.fda.gov/downloads/Drugs/DrugSafety/InformationbyDrugClass/UCM173233.pdf>> [Accessed: 11 June 2011].

[These changes should be made to the box warning at the beginning of the package insert.]

DRUG NAME

Suicidality and Antidepressant Drugs

Antidepressants increased the risk compared to placebo of suicidal thinking and behavior (suicidality) in children, adolescents, and young adults in short-term studies of major depressive disorder (MDD) and other psychiatric disorders. Anyone considering the use of [Insert established name] or any other antidepressant in a child, adolescent, or young adult must balance this risk with the clinical need. Short-term studies did not show an increase in the risk of suicidality with antidepressants compared to placebo in adults beyond age 24; there was a reduction in risk with antidepressants compared to placebo in adults aged 65 and older. Depression and certain other psychiatric disorders are themselves associated with increases in the risk of suicide. Patients of all ages who are started on antidepressant therapy should be monitored appropriately and observed closely for clinical worsening, suicidality, or unusual changes in behavior. Families and caregivers should be advised of the need for close observation and communication with the prescriber. [Insert Drug Name] is not approved for use in pediatric patients. [The previous sentence would be replaced with the sentence, below, for the following drugs: Prozac: Prozac is approved for use in pediatric patients with MDD and obsessive compulsive disorder (OCD). Zoloft: Zoloft is not approved for use in pediatric patients except for patients with obsessive compulsive disorder (OCD). Fluvoxamine: Fluvoxamine is not approved for use in pediatric patients except for patients with obsessive compulsive disorder (OCD).] (See Warnings: Clinical Worsening and Suicide Risk, Precautions: Information for Patients, and Precautions: Pediatric Use)

[The following changes should be made to the current language under the **WARNINGS-Clinical Worsening and Suicide Risk** section.]

WARNINGS-Clinical Worsening and Suicide Risk

Patients with major depressive disorder (MDD), both adult and pediatric, may experience worsening of their depression and/or the emergence of suicidal ideation and behavior (suicidality) or unusual changes in behavior, whether or not they are taking antidepressant medications, and this risk may persist until significant remission occurs. Suicide is a known risk of depression and certain other psychiatric disorders, and these disorders themselves are the strongest predictors of suicide. There has been a longstanding concern, however, that

antidepressants may have a role in inducing worsening of depression and the emergence of suicidality in certain patients during the early phases of treatment. Pooled analyses of short-term placebo-controlled trials of antidepressant drugs (SSRIs and others) showed that these drugs increase the risk of suicidal thinking and behavior (suicidality) in children, adolescents, and young adults (ages 18-24) with major depressive disorder (MDD) and other psychiatric disorders. Short-term studies did not show an increase in the risk of suicidality with antidepressants compared to placebo in adults beyond age 24; there was a reduction with antidepressants compared to placebo in adults aged 65 and older.

The pooled analyses of placebo-controlled trials in children and adolescents with MDD, obsessive compulsive disorder (OCD), or other psychiatric disorders included a total of 24 short-term trials of 9 antidepressant drugs in over 4400 patients. The pooled analyses of placebo-controlled trials in adults with MDD or other psychiatric disorders included a total of 295 short-term trials (median duration of 2 months) of 11 antidepressant drugs in over 77,000 patients. There was considerable variation in risk of suicidality among drugs, but a tendency toward an increase in the younger patients for almost all drugs studied. There were differences in absolute risk of suicidality across the different indications, with the highest incidence in MDD. The risk differences (drug vs placebo), however, were relatively stable within age strata and across indications. These risk differences (drug-placebo difference in the number of cases of suicidality per 1000 patients treated) are provided in Table [add table number].

Table [add table number]	
Age Range	Drug-Placebo Difference in Number of Cases of Suicidality per 1000 patients Treated
	Drug-Related Increases
<18	14 additional cases
18-24	5 additional cases
	Drug-Related Decreases
25-64	1 fewer case
>65	6 fewer cases

No suicides occurred in any of the pediatric trials. There were suicides in the adult trials, but the number was not sufficient to reach any conclusion about drug effect on suicide.

It is unknown whether the suicidality risk extends to longer-term use, i.e., beyond several months. However, there is substantial evidence from placebo-controlled maintenance trials in adults with depression that the use of antidepressants can delay the recurrence of depression.

All patients being treated with antidepressants for any indication should be monitored appropriately and observed closely for clinical worsening, suicidality, and unusual changes in behavior, especially during the initial few months of a course of drug therapy, or at times of dose changes, either increases or decreases.

The following symptoms, anxiety, agitation, panic attacks, insomnia, irritability, hostility, aggressiveness, impulsivity, akathisia (psychomotor restlessness), hypomania, and mania, have been reported in adult and pediatric patients being treated with antidepressants for major depressive disorder as well as for other indications, both psychiatric and nonpsychiatric.

Although a causal link between the emergence of such symptoms and either the worsening of depression and/or the emergence of suicidal impulses has not been established, there is concern that such symptoms may represent precursors to emerging suicidality.

Consideration should be given to changing the therapeutic regimen, including possibly discontinuing the medication, in patients whose depression is persistently worse, or who are experiencing emergent suicidality or symptoms that might be precursors to worsening depression or suicidality, especially if these symptoms are severe, abrupt in onset, or were not part of the patient's presenting symptoms.

[The labeling for the following drugs with discontinuation language would include the next paragraph: Celexa, Cymbalta, Effexor, Fluvoxamine, Lexapro, Paxil, Pexeva, Prozac, Sarafem, Symbyax, and Zoloft.]

If the decision has been made to discontinue treatment, medication should be tapered, as rapidly as is feasible, but with recognition that abrupt discontinuation can be associated with certain symptoms (see PRECAUTIONS and DOSAGE AND ADMINISTRATION—Discontinuation of Treatment with [Insert established name], for a description of the risks of discontinuation of [Insert established name]).

Families and caregivers of patients being treated with antidepressants for major depressive disorder or other indications, both psychiatric and nonpsychiatric, should be alerted about the need to monitor patients for the emergence of agitation, irritability, unusual changes in behavior, and the other symptoms described above, as well as the emergence of suicidality, and to report such symptoms immediately to health care providers. Such monitoring should include daily observation by families and caregivers. Prescriptions for [Insert Drug Name] should be written for the smallest quantity of tablets consistent with good patient management, in order to reduce the risk of overdose.

Screening Patients for Bipolar Disorder: A major depressive episode may be the initial presentation of bipolar disorder. It is generally believed (though not established in controlled trials) that treating such an episode with an antidepressant alone may increase the likelihood of precipitation of a mixed/manic episode in patients at risk for bipolar disorder. Whether any of the symptoms described above represent such a conversion is unknown. However, prior to initiating treatment with an antidepressant, patients with depressive symptoms should be adequately screened to determine if they are at risk for bipolar disorder; such screening should include a detailed psychiatric history, including a family history of suicide, bipolar disorder, and depression. It should be noted that [Insert Drug Name] is not approved for use in treating bipolar depression. [The previous sentence would be replaced for the following drugs: Seroquel: It should be noted that Seroquel is approved for use in treating adult bipolar depression. Symbyax: It should be noted that Symbyax is approved for use in treating adult bipolar depression.

[The following changes should be made in current language under the PRECAUTIONS-Information for Patients section.]

PRECAUTIONS-Information for Patients

Prescribers or other health professionals should inform patients, their families, and their caregivers about the benefits and risks associated with treatment with [Insert Drug Name] and should counsel them in its appropriate use. A patient Medication Guide about “Antidepressant Medicines, Depression and other Serious Mental Illness, and Suicidal Thoughts or Actions” is available for [Insert Drug Name]. The prescriber or health professional should instruct patients, their families, and their caregivers to read the Medication Guide and should assist them in understanding its contents. Patients should be given the opportunity to discuss the contents of the Medication Guide and to obtain answers to any questions they may have. The complete text of the Medication Guide is reprinted at the end of this document.

Patients should be advised of the following issues and asked to alert their prescriber if these occur while taking [Insert Drug Name].

Clinical Worsening and Suicide Risk: Patients, their families, and their caregivers should be encouraged to be alert to the emergence of anxiety, agitation, panic attacks, insomnia, irritability, hostility, aggressiveness, impulsivity, akathisia (psychomotor restlessness), hypomania, mania, other unusual changes in behavior, worsening of depression, and suicidal ideation, especially early during antidepressant treatment and when the dose is adjusted up or down. Families and caregivers of patients should be advised to look for the emergence of such symptoms on a day-to-day basis, since changes may be abrupt. Such symptoms should be reported to the patient's prescriber or health professional, especially if they are severe, abrupt in onset, or were not part of the patient's presenting symptoms. Symptoms such as these may be associated with an increased risk for suicidal thinking and behavior and indicate a need for very close monitoring and possibly changes in the medication.

Appendix E

WHO Atlas Project Participants

Information collated from:

WHO, 2005b. *Atlas: child and adolescent mental health resources: global concerns, implications for the future*. Geneva: World Health Organization.

Member States of the WHO by Region⁸:

WHO region	Participating countries
Africa	Algeria , Angola, Benin , Botswana, Burkina Faso , Burundi, Cameroon, Cape Verde, Central African Republic, Chad, Comoros, Congo , Côte d'Ivoire, Democratic Republic of the Congo, Equatorial Guinea, Eritrea , Ethiopia , Gabon , Gambia, Ghana, Guinea , Guinea-Bissau , Kenya , Lesotho, Liberia, Madagascar , Malawi, Mali, Mauritania, Mauritius, Mozambique, Namibia, Niger , Nigeria, Rwanda, Sao Tome and Principe, Senegal , Seychelles, Sierra Leone, South Africa, Swaziland, Togo, Uganda, United Republic of Tanzania, Zambia , Zimbabwe
Americas	Antigua and Barbuda, Argentina , Bahamas, Barbados, Belize, Bolivia, Brazil , Canada, Chile , Colombia , Costa Rica, Cuba, Dominica, Dominican Republic, Ecuador, El Salvador, Grenada, Guatemala , Guyana, Haiti, Honduras, Jamaica , Mexico , Nicaragua, Panama, Paraguay , Peru, Saint Kitts and Nevis, Saint Lucia, Saint Vincent and the Grenadines, Suriname, Trinidad and Tobago, United States of America, Uruguay , Venezuela
South-East Asia	Bangladesh, Bhutan, Democratic People's Republic of Korea, India , Indonesia, Maldives, Myanmar, Nepal, Sri Lanka , Thailand , Timor-Leste
Europe	Albania, Andorra, Armenia, Austria , Azerbaijan, Belarus, Belgium , Bosnia and Herzegovina, Bulgaria, Croatia , Cyprus, Czech Republic , Denmark , Estonia , Finland , France, Georgia, Germany , Greece , Hungary, Iceland , Ireland, Israel , Italy , Kazakhstan, Kyrgyzstan, Latvia , Lithuania , Luxembourg, Malta, Monaco, Netherlands, Norway , Poland, Portugal , Republic of Moldova, Romania , Russian Federation , San Marino, Serbia and Montenegro, Slovakia , Slovenia , Spain, Sweden , Switzerland , Tajikistan, The former Yugoslav Republic of Macedonia, Turkey , Turkmenistan, Ukraine, United Kingdom , Uzbekistan

⁸ Countries in **bold** participated in the *Child Mental Health Atlas*.

Eastern Mediterranean	Afghanistan, Bahrain , Djibouti, Egypt , Iran (Islamic Republic of) , Iraq, Jordan , Kuwait, Lebanon , Libyan Arab Jamahiriya, Morocco, Oman, Pakistan, Qatar, Saudi Arabia, Somalia, Sudan , Syrian Arab Republic, Tunisia , United Arab Emirates , Yemen
Western Pacific	Australia, Brunei Darussalam, Cambodia, China (and Hong Kong SAR) , Cook Islands, Fiji, Japan , Kiribati, Lao People's Democratic Republic , Malaysia , Marshall Islands, Micronesia (Federated States of), Mongolia, Nauru, New Zealand, Niue, Palau, Papua New Guinea, Philippines, Republic of Korea , Samoa, Singapore, Solomon Islands, Tonga, Tuvalu, Vanuatu, Viet Nam

Countries included in the *Child Mental Health Atlas*:

WHO region	Total number of countries	Atlas questionnaire received from countries	Population of responding countries (percent)
Africa	46	15 (32.7%)	34.4%
Americas	35	9 (25.7)	46.9%
South-East Asia	11	3 (27.3%)	71.1%
Europe	52	25 (48.1%)	64.7%
Eastern Mediterranean	21	8 (38.1%)	38.5%
Western Pacific	27	6 (22.2%)	87.7%
World⁹	192	66 (34.4%)	

⁹ World statistics based on information found in *Child Atlas*.

Appendix F

Interview Outline

Hello, as previously stated, my name is Molly Deacutis, and I am working on my Master of Philosophy degree in Neuroscience at the University of St Andrews. I am here in (state location) to speak with you today, (state date), in order to gather a professional perspective concerning the diagnosis and treatment of children and adolescents with mental health disorders, particularly depression. The information we will discuss may be included in my thesis to support the literature research I have collected, as well as provide data for the possibility of related publications. All this information is included for you on the information sheet and debriefing form, as well. I would like to thank you again for taking the time to talk to me today.

Before we get started, can you please state your clinical position?

Now, the first major topic of my research concerns the process of diagnosing children; that is, classifying or labelling patients with a specific disorder or disorders. As mentioned before, diagnosis is not commonly used at this clinic; why is this the practice? Why is diagnosis used in certain cases and not others? What is the purpose of diagnosing?

When diagnosis is used, what method is used to determine a patient's diagnosis? A checklist based on the diagnostic criteria set out by the ICD (or other diagnostic system)? A written evaluation? Etc?

I'm also interested in why children are being brought in for treatment. How self aware of their disorder do your patients seem? How much is treatment sought more based on the observation of parents, teachers, or others?

My research also looks at the impact of mental health disorders and treatment on children's development of identity, how children view themselves in the context of their world, as well as a development of autonomy, an understanding of self-control. How much of an impact on a patient's identity do you notice following a diagnosis/treatment or by the disorder itself? And how much of an impact do you notice on their sense of autonomy?

What is the most common disorder(s) that comes into your clinic? And what is the most common disorder that you see? (Do you have a specialization?)

The other major topic in my research is paediatric treatment. Of the patients that you see, approximately what percentage is medicated for a mental health disorder? And approximately what percentage of your patients do you prescribe medication for?

Which drugs are most commonly prescribed at this clinic? Which drugs do you most commonly prescribe?

And as my thesis focuses on depression as a case study, which antidepressants are most commonly prescribed here? And which antidepressants do you most commonly prescribe?

Over the past six years, there has been a change in antidepressant guidelines recommending only the prescription of fluoxetine to young people between the ages of 18-25 due to increased risk of suicidality related to SSRI use. How has this change impacted medication practices in your clinic and/or by you, if at all?

Also suggested by these guidelines has been using psychotherapy (CBT) as the frontline treatment, followed by fluoxetine as a first-line medication treatment, and only then to use other antidepressants as second-line treatment. In reality, what is the treatment plan used in this clinical practice? If real practices differ from the guidelines, what are the pressures causing those discrepancies?

In general, what are the common symptoms that you see in depressed patients? Do you see variation based on age/gender?

Lastly, while the NHS focuses only on treating impairment, do you think it is plausible that neuroenhancement may become widespread practice in coming years?

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