Research Review
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Treatment Decisions in Schizophrenia and Differentiating ADHD from Bipolar Disorder
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Professor Keith is the immediate past editor of Academic Psychiatry, the former editor of the Schizophrenia Bulletin and serves on the editorial advisory boards of Biological Therapies in Psychiatry Newsletter, the Journal of Clinical Psychiatry and the Journal of Psychiatric Rehabilitation. He has served on numerous national committees and advisory boards including the DSM III-R and DSM-IV Work Groups on Schizophrenia and has published widely on the treatment and diagnosis of schizophrenia.

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Dr Mastroianni is a registered medical practitioner in New South Wales (NSW) and a registered consultant psychiatrist in both the private and public sectors. After gaining his Bachelor of Medicine and Bachelor of Surgery from Sydney University, Dr Mastroianni completed his postgraduate psychiatric training in Sydney. Dr Mastroianni is a Fellow of the Royal Australian and New Zealand College of Psychiatrists. He has also completed postgraduate fellowship training in forensic psychiatry at the Institute for Forensic Psychiatry in Michigan, USA and postgraduate training in Italian general psychiatry at the University of Pavia, Italy.

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This publication summarises recent presentations by Professor Samuel J. Keith regarding current thinking on long-acting antipsychotic injections in schizophrenia and by Dr Tony Mastroianni on differentiating attention-deficit hyperactivity disorder from bipolar disorder. They spoke to panels of psychiatrists and health professionals in Auckland, Hamilton, Wellington and Christchurch.

Current thinking on long-acting injections: rational, irrational or rationalisation?

Professor Keith highlighted the top 10 rationalisations used by health professionals when considering long-acting antipsychotic injections in the treatment of schizophrenia.

1. Our patients take the medications we prescribe

On the contrary, nonadherence to medication has been a concern for over 2000 years, with Hippocrates in 200 B.C. advising physicians to be alert for problems with adherence. Notably, compliance rates are low in chronic disease states such as asthma and rheumatoid arthritis (approximately 40% of patients in each disease state are fully adherent, about 40% are partially adherent and around 20% are not taking their medications),[1,2] but are even lower in schizophrenia. Two separate studies have found that both patients with schizophrenia and clinicians overestimate compliance. Whereas 67.5% of patients stated they had taken all of their doses over 3 months, a pill count revealed that only 10.3% of patients were fully compliant.[3] As for the clinicians, their best estimate of the proportion of their outpatients who missed ≥30% of their medication was approximately 6%, whereas an electronic monitoring device in the medication bottle caps showed that 61.9% of the patients met this threshold for noncompliance.[4]

2. Atypicals have solved the poor compliance issue

The introduction of the new second-generation antipsychotics was hailed as the solution to the compliance issue; it was predicted that patients would want to take these drugs with much lower rates of treatment-emergent extrapyramidal symptoms (EPS). However, data indicate otherwise. In one study, as few as 5.2% of 349 patients with schizophrenia receiving risperidone and 7.1% of 326 receiving conventional antipsychotics were on continuous medication over the course of one year; with 94.8% and 92.9% of patients, respectively, receiving no antipsychotic therapy for a substantial portion of the study (110.2 and 125.0 days for risperidone and conventional antipsychotics, respectively), enough to cause serious clinical problems.[5]

3. A few days without medication can't matter

In fact, missing even only a few days of antipsychotic doses has serious consequences. In a review of California Medicaid pharmacy refill and medical claims for 4,325 outpatients for whom antipsychotics were prescribed for treatment of schizophrenia from 1999 to 2001, the risk of hospitalisation was significantly correlated with compliance.[6] Having any gap in medication coverage increased the risk of hospitalisation, including a gap as small as between 1 and 10 days (odds ratio [OR]=1.98) [see Figure 1 on page 2]. A gap of 11 to 30 days was associated with an OR of 2.81, and a gap of >30 days was associated with an OR of 3.96.

The large impact that even just a small gap of medication coverage has upon hospitalisation rates has been attributed to the treatment paradigm evolving from one of megadosing and rapid neuroleptisation to one that favours the lowest effective dose. While the lowest effective dose maintains side effects to a minimum, missing even a few days of medication means that the patient is below the threshold for clinical response.

4. Our patients tell us when they aren't taking their medications

As Lam and colleagues have demonstrated, as many as 68% of patients will claim that they are taking all their medications, when pill counts indicate that only 10% of patients are compliant.[3]

5. We know when our patients aren't taking their medications

Notably, Byerly and colleagues found that up to 95% of clinicians will predict that their patients are taking over 70% of their medications as prescribed, when electronic monitoring of medication doses showed that only 38% of those patients were compliant.[4] This is probably an overestimation of drug use. In a different therapeutic area, a US-based study that used electronic monitoring devices to record inhaler use during the 90-day intervals between appointments among Veterans Affairs patients with chronic obstructive pulmonary disease showed that 30% of their inhaler usage was in the last 3 hours before their next appointment.[7]

6. Patients won't take injections

A commonly voiced objection to injectable antipsychotics contends that few if any patients with schizophrenia will want to receive medication by injection. However, research suggests that those patients who have had experience with long-acting injections often prefer them. In a review of patient and nurse attitudes regarding depot antipsychotics, 5 of 6 studies comparing depot with oral medication showed patient preference for depot [see Figure 2].[8] The sixth study showed a patient preference for oral medication, but this was a second-generation oral against a first-generation long-acting injectable (LAI). Patients like the second-generation drugs, but they do not take them very well.

Long-term data have shown that more patients stay on long-acting injectables compared with oral medications, with 82% of patients receiving risperidone long-acting injectable (RLAI) therapy being successfully retained for 24 months compared with 63% of patients receiving oral risperidone or olanzapine.[9]

7. Continuous medication is not necessary; we can always turn prodromal symptoms around with vigorous interventions

The evidence states otherwise. In an analysis of five long-term studies comparing continuous treatment with targeted treatment given only when patients showed early signs of clinical worsening, rates of relapse after 1 year were much lower for those on continuous therapy versus those given targeted therapy.[10] This occurred despite very close patient monitoring; physicians could not intervene fast enough with targeted medication.

8. There is no advantage to an injectable – it is really the same drug

This viewpoint is not supported by the evidence. In six studies that compared the number of hospitalisations when patients were solely on oral medication with the number occurring after initiation of depot medication, the rate of relapse was reduced by depot medication in five of the studies [see Figure 3].[11] Another advantage of LAIs is that their continuous medication delivery is likely to improve long-term treatment outcomes. Gharabawi and colleagues observed improvements in stable patients switched from oral risperidone to long-acting risperidone, including improvements in Positive and Negative Syndrome Scale (PANSS) scores, a gradual decline in EPS and decrease in the use of antiparkinsonian medications (from >20% to <2%).[12]

Notably, fluctuations in plasma drug levels and peak plasma drug levels are considerably lower with long-acting risperidone than with the oral form, indicating that the

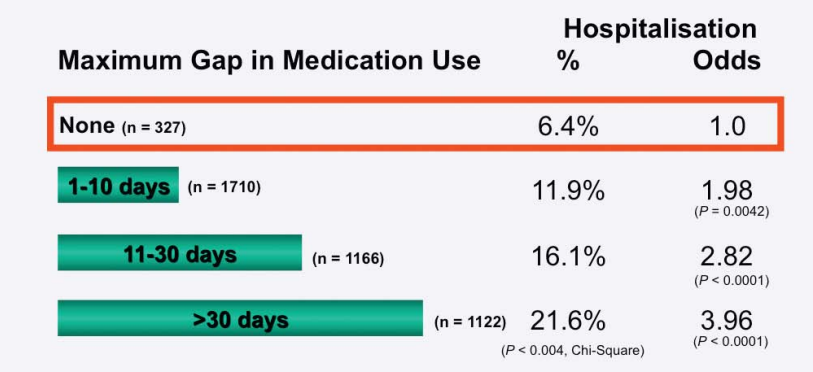

Figure 1. California Medicaid results: hospitalisation by maximum gap[6]

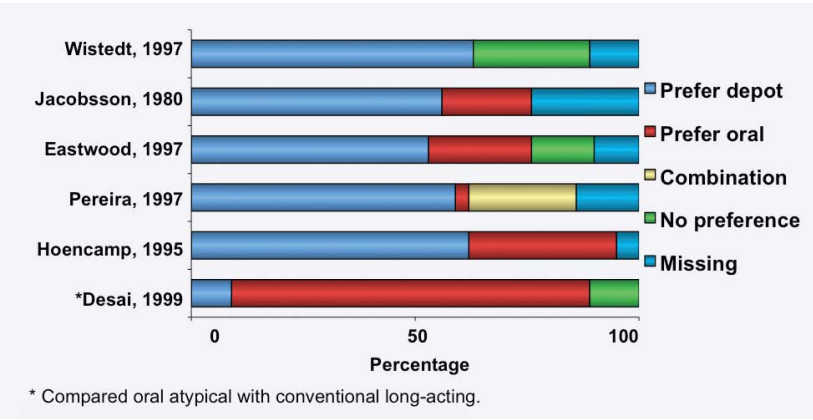

Figure 2. Patients often prefer long-acting antipsychotics[8]

Study	Number of subjects	Study duration	Relapsed (%) Oral	Relapsed (%) Depot	Difference in Relapse Rates (oral minus depot) (%)
Crawford and Forest (1974)	29	40 weeks	27	0	27
del Guidice et al (1975)	82	1 year	91	43	48
Rifkin et al (1977)	51	1 year	11	9	2
Falloon et al (1978)	41	1 year	24	40	-16
Hogarty et al (1979)	105	2 years	65	40	24
Schooler et al (1979)	214	1 year	33	24	9

Mantel-Haenszel: $P < 0.0002$.

Figure 3. Potential to improve relapse rates with depot vs oral antipsychotics[11]

injectable formulation provides more consistent and predictable plasma drug levels [see Figure 4 on page 3].[13] The peaks that occur with every oral dose drive receptor-mediated side effects such as EPS and prolactin levels; side effects that improve with RLAI dosing. For example, when 257 patients with schizophrenia symptomatically stable on oral risperidone were switched to LAI risperidone for 12 weeks, mean prolactin levels were significantly decreased from 37.4 mg/mL at baseline to 32.6 ng/mL at endpoint ($p<0.001$), whereas in the oral risperidone group (n=276), levels were essentially unchanged from baseline to endpoint (38.9 ng/mL to 38.0 ng/mL; p=0.301).[14]

9. Early-episode patients couldn't tolerate injectables

This rationalisation includes statements such as "They won't accept them" and "They'd get EPS". Recently released data have proven that these concerns are unjustified. The effects of oral antipsychotics versus RLAI treatment were compared between two similar studies lasting 2 years

each in patients with early-episode psychosis.[15] The findings of this post hoc analysis suggest that there were advantages in terms of fewer all-cause discontinuations, greater reduction on the PANSS-Total score, higher remission rate and lower relapse rate among the responders in the RLAI group, compared with responders in the oral antipsychotic treatment groups. In addition, significantly fewer EPS episodes occurred with RLAI than with oral risperidone or haloperidol.

In another study involving 51 patients with first-episode schizophrenia, LAI-treated patients had significantly higher medication adherence than patients on oral medication; only the fully adherent patients (i.e. defined as taking >73% of the medication) showed any improvement at all, as assessed by PANSS and Brief Psychiatric Rating Scale (BPRS) scores.[16]

Importantly, early pharmacotherapy and psychotherapy reduces the risk of early transition to psychosis in patients with subthreshold symptoms of schizophrenia. In a randomised controlled trial that enrolled 59 patients at incipient risk of progression to first-episode psychosis (family history of psychosis in a 1st degree relative, non-specific symptoms, decline of 30 points on Global Assessment of Functioning in past 12 months, with attenuated positive symptoms for at least a week, but remaining below the threshold of frank psychosis), needs-based intervention was compared with specific preventive intervention comprising low-dose risperidone therapy (mean dosage, 1.3 mg/day) and cognitive behaviour therapy (CBT).[17] Treatment was provided for 6 months, after which all patients were offered ongoing needs-based intervention. Outcomes were assessed at 6 and 12 months. By the end of treatment, 10 of 28 people who received needs-based intervention progressed to first-episode psychosis vs 3 of 31 from the specific preventive intervention group (p=0.03). After 6 months' follow-up, another 3 people in the specific preventive intervention group became psychotic, and with intention-to-treat analysis, the difference was no longer significant (p=0.24). However, for risperidone therapy-adherent patients in the specific preventive intervention group, protection against progression extended for 6 months after cessation of risperidone use. CBT alone with poorly adherent risperidone-treated patients was unable to prevent the development of psychosis.

10. The course of schizophrenia is invariably downhill

Unfortunately, a lot of data support this statement. In 1999, Bromet and Fennig studied the course of illness in patients with first-episode psychosis entering a treatment facility in Suffolk County, Long Island.[18] When these people were followed-up 3 to 5 years later, only 5.2% experienced a single episode and achieved a complete remission. Approximately 15% experienced a single episode and an incomplete remission, while about 80% had multiple episodes or remained continuously ill.

Is remission too much to hope for in schizophrenia? A recently proposed definition of remission requires the simultaneous attainment of a score of 3 (mild), 2 (minimal), or 1 (absent) for at least 6 months for all of 8 PANSS items [see Figure 5].[19]

Lasser and colleagues applied these criteria for remission to a one-year-long study of RLAI, in which 578 stable patients with schizophrenia or schizoaffective disorder received RLAI every 2 weeks.[20] At baseline, 184 patients met the symptom-severity criteria for remission. Of the 394 patients who did not meet the symptom-severity component of the remission criteria at baseline, 82 (20.8%) achieved symptom remission for ≥6 months, with significant decreases in mean PANSS-Total and cluster scores and significantly improved patient-rated health status as assessed by the 36-Item Short-form Health Survey (SF-36), with a substantial increase from baseline to endpoint in the proportion of patients who met US SF-36 norms. In addition, the percentages rated as not ill, very mild, or mild on Clinical Global Impression-Severity ratings increased from 39% to 88%. One-hundred fifty-six (84.8%) of the 184 patients meeting the symptom-severity

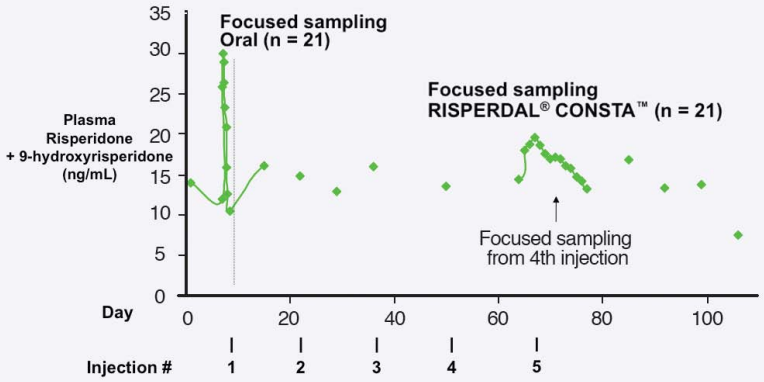

Figure 4. Risperdal® Consta®: Lower peak plasma levels vs oral risperidone[13]

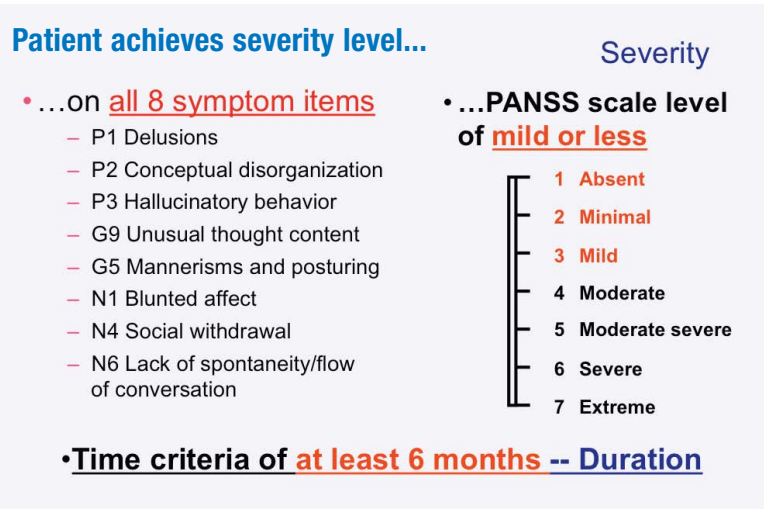

Figure 5. Remission criteria in schizophrenia[19]

component of remission criteria at baseline maintained these criteria at endpoint. Although these 156 patients had very low mean total PANSS scores at baseline, further significant symptom improvements were observed, with a reduction from a mean total PANSS of 47.8 at baseline to 43.4 at endpoint. Thus, many of the previously "stable" nonremitted patients achieved symptom remission after RLAI treatment and many of those who met the remission criteria at baseline were able to maintain these criteria at endpoint.

Summary

Is our thinking rational in regard to long-acting antipsychotic injections? We rationalise that our patients take the medications we prescribe, despite the fact that high numbers of patients are noncompliant with antischizophrenic medications. Notably, atypical agents are not the answer to poor compliance, with the majority of treated patients remaining poorly adherent. Significantly, missing even only a few days of medication greatly increases the risk of hospitalisation. Pill counts contradict patients who state they are taking their medications and electronic monitoring devices prove us to be mistaken when we believe our patients to be compliant with therapy. Evidence demonstrates that patients often prefer depot over oral antipsychotic formulations and that they are successfully retained for a longer time on RLAI than on oral treatment. Relapse rates are much higher in patients given targeted treatment for prodromal symptoms compared with relapse rates among patients on continuous therapy. Improvements in relapse rates, side effects and more predictable plasma drug levels have been recorded after switching patients from oral risperidone to the LAI formulation. Many therapeutic advantages have been recorded with LAI treatment over oral treatment in early-episode patients. The course of schizophrenia is not a consistently downhill course; symptom remission is possible upon RLAI therapy. In the face of the evidence, are our rationalisations simply excuses to avoid using LAIs?

Differentiating ADHD from bipolar disorder

Much controversy surrounds these disorders. Worldwide, there is increased community awareness and media focus on famous people with these disorders such as Michael Phelps, known to have attention-deficit hyperactivity disorder (ADHD) and Britney Spears, widely speculated to have bipolar disorder. Patients are more often asking for a definite diagnosis, to know with certainty what illness they have. However, they do not necessarily present with a neatly diagnosable condition. Instead, they present with complex affective, behavioural, cognitive, learning, personality and substance abuse difficulties. Classificatory symptoms used in psychiatry (e.g. DSM) are of minimal help in ADHD and bipolar disorder. Diagnoses are based on a heterogeneous set of symptoms that cause impairment and the impairments are dimensional (e.g. Bipolar I, II and not otherwise specified; ADHD – Hyperactive, Inattentive, Combined types). No gold standard tests exist for diagnoses and there is considerable overlap of symptoms between diagnoses.

Ultimately, the problem is that misdiagnosis can cause harm. It is the duty of physicians to be clear about diagnosis and treatment in order to inform patients about their conditions. Treatment can directly cause harm (e.g. trigger a manic or psychotic episode). Physicians can also cause harm by missing a diagnosis. Patients may seek clarification as to whether they have ADHD as a means of improving their self-understanding. To be told that they have or do not have ADHD, or that ADHD does not even exist, has important ramifications for them.

DSM classifications

The classificatory systems used by DSM for ADHD and bipolar disorder are very different, on the surface. So why are we even discussing whether we have to make a distinction? Bipolar disorder is after all a distinct entity, with periods where the person may be able to talk in a distractible state and is hyperaroused. ADHD is lifelong, starts before the age of 7 years, and comprises a pervasive set of symptoms.

Prevalence estimates depend on the diagnostic criteria used and thus vary widely, from 1.7% to 17.8% for ADHD, and in bipolar disorder, range from 1% in adolescence to 2% in adults and up to 5% for subsyndromal bipolar disorder.[21-23] Controversy exists in the commonly observed co-morbidities.

Interestingly, when those individuals who have ADHD and co-morbid antisocial personality disorder are excluded, the remaining 75% of people with ADHD do not have behavioural problems (stereotypically associated with ADHD) significantly higher than the general population.

However, up to 10% of adults with ADHD also meet the criteria for bipolar disorder. Importantly, most childhood bipolar patients will meet criteria for ADHD. Dr. Mastroianni noted that in his forensic psychiatry work, he often encounters patients with mental illness and substance abuse disorders, who were diagnosed with ADHD in childhood and treated with stimulants. Like many psychiatrists, he had traditionally conceptualised that the childhood ADHD in those individuals was, in hindsight, a manifestation of an emerging Axis I serious mental illness. After considering the extensive research, he now questions whether this diagnostic paradigm is true for all such patients.

Co-morbidity common:

ADHD:	50% substance abuse disorder
	25% conduct/antisocial personality disorder
	30% anxiety disorder
	10% bipolar disorder
	20% depressive disorder
	10% learning disability
Bipolar Disorder:	50% substance abuse disorder
	10-15% suicide
	60–90% childhood bipolar have ADHD
	10% adult bipolar have ADHD
	30% anxiety disorder
	20% personality disorder

Considerable overlap

In the real world, considerable overlap exists between ADHD and bipolar disorder, personality disorder, substance abuse, and anxiety disorders [see Figure 1]. Where do we place any given patient within this spectrum? It is important to remember that in psychiatry, every diagnosis – not just ADHD or bipolar disorder – presents with attentional difficulties. Disorders with attention difficulties include major depression/chronic dysthymia, the prodromal and negative symptoms associated with the schizophrenia spectrum, medical disorders such as thyroid disease, sleep apnoea, narcolepsy and Tourettes, post-traumatic stress disorder, anxiety disorders (e.g. obsessive-compulsive disorder, generalised anxiety disorder), substance intoxication/withdrawal, auditory/visual processing difficulties, pervasive developmental disorders and specific learning disorder, amongst others. How do we distinguish between all of these? How do we best conceptualise the disorder for the patient and decide on treatment?

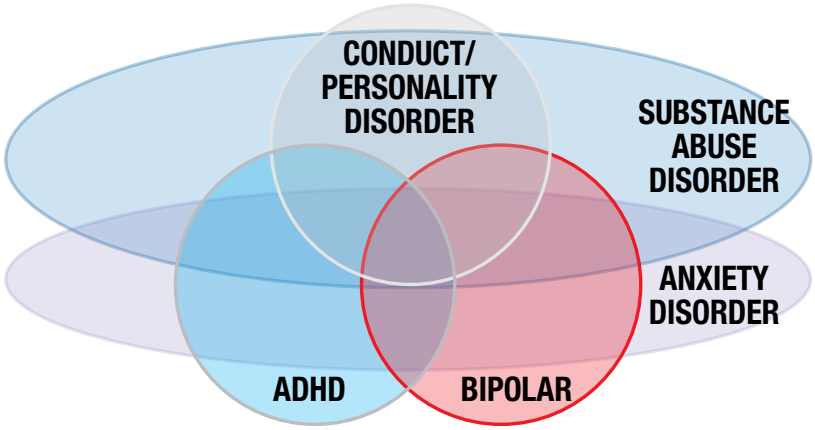

Figure 1. Co-morbidity

Conceptualising the disorder of inattention

Dr. Mastroianni uses the analogy of the "front line" and "back line" of an army in warfare as a means of conceptualising the brain's ability to concentrate on a particular task. ADHD can be simply conceptualised as sitting within the frontal lobes (the brain's "front line"), which are responsible for executive functioning, inhibition, planning and working memory.

The frontal lobes' ability to attend to a task is affected by background structures in the brain (the brain's "back line") such as the reticular activating system, mesolimbic system, thalamus, temporal lobe, etc. Any deficits or disorders affecting these "back line" structures will impact on the brain's attentional capacity. Clinicians need to delineate which structures are contributing to a patient's presentation in order to clarify the co-morbid diagnoses and to tailor management accordingly. It is useful for patients to understand this concept to enable them to take responsibility for their own management. For example, a patient with ADHD may understand why the stimulant medication no longer appears to be working when poor sleep affects the reticular activating system, or is enhanced by techniques to identify the salience of a task that activates the mesolimbic system.

Clinical presentations

Certain features of bipolar disorder can be distinguished from features associated with ADHD. For instance, hypersexuality is a feature of childhood bipolar disorder but is not normally seen in ADHD, unless there is acting out from a co-morbid sexual abuse history. Bipolar disorder is also marked by irritability and aggressive behaviour, increased activity, severe mood shifts and liability, rapid cycling, psychosis, and pressured speech. In ADHD, the irritable mood component is brief and usually related to frustration. ADHD is not really a conduct problem, unless the individual has a co-morbid conduct disorder. The mental state for ADHD is very different from that for bipolar disorder. It is important to remember that at whatever age a child starts to present with bipolar disorder, the presentations differ markedly from the individual's normal behaviour or state of functioning, whereas presentations in ADHD represent the child's normal functioning, from before the age of 7 years.

The DSM-IV symptom domain is not so helpful for classifying adults with ADHD, as the criteria are really designed for children.[24] The hyperactivity that marks childhood ADHD often transforms into inner restlessness in adulthood. Commonly, adult ADHD is marked by workaholism, constant overscheduling and a feeling of being overwhelmed. There is self-selection into active roles such as sales and marketing, advertising, the stockmarket, as well as a constant level of activity that affects family members, with constant tension in the household.

Symptoms of impulsivity often manifest differently in adults than they do in children. Children who meet the DSM-IV criteria for impulsivity will blurt out answers, cannot wait for a turn, intrude on/interrupt others.[24] In adulthood, impulsivity manifests as a chronic low frustration tolerance; individuals typically lose their temper quickly, quit jobs impulsively, end relationships, drive too fast, and have an addictive personality.[25]

Similarly, symptoms of inattention tend to manifest differently in adults. The DSM-IV domain lists symptoms as difficulty in sustaining attention, failure to listen, no follow through, an inability to organise, losing important items, distractibility and forgetfulness.[24] Inattention in adults presents as chronic poor time management, inefficiency, paralysing procrastination, and difficulty in sustaining attention during meetings, reading and paperwork.[25]

The cognitive aspects of ADHD do improve with age, although they plateau at around the age of 30 years. However, they carry more significant morbidity, because of the increased demands on the frontal lobe in adulthood. In childhood, the parents, school, and games coaches all act as the child's frontal lobes in a protective environment, whereas adults have to manage with competing tasks, independence, and the necessities of organisation and planning. Thus, executive functions become more important in adulthood and are easily overwhelmed despite improved ADHD.

Genetics

Is there a common genetic base between ADHD and bipolar disorder? Both are highly inheritable disorders, particularly ADHD [see Figure 2]. Of interest is the increased risk of ADHD among offspring of individuals with bipolar disorder and the increased risk of bipolar disorder among ADHD offspring, suggestive of a genetic similarity. However, not one recognised gene exists in common between the two disorders. In fact, the genes found in bipolar disorder more closely resemble those found in schizophrenia.

ADHD

- Risk for first degree relatives up to 8 times higher than gen. population
- Monozygotic twin concordance rate at 76% (v.high)
- Increased risk of Bipolar Disorder in ADHD offspring
- Genes, possibly: Dopamine transporter gene, DRD2, DRD4, Dopamine Beta-Hydroxylase gene, 5-HTT, Serotonin transporter gene, norepinephrine transporter gene.

Bipolar Disorder

- Risk for first degree relatives up to 4- 6 times higher (esp. early onset, high co-morbidity)
- Increased risk of ADHD in Bipolar offspring
- Genes, possibly: BDNF, G72, AKT1, GRIN2A, XBP1, GRK3, HTR4, IMPA2, GABRA 1, DRD3, Glutamatergic and mitochondrial dysfunction.

NB: Gene variant, which codes for a dopamine receptor (DRD4 7-repeat allele) associated with thinning of cortex and ADHD children with this variant eventually remitted closer to non-ADHD by adulthood (Shaw et.al 2007)

Figure 2. Genetics

ADHD

- Reduced Dopamine D2 receptor density in prefrontal cortex.
- Reduced blood flow in frontal lobes when doing complex tasks. Stimulants increase flow.
- Thinner temporal lobe cortex.
- Grey matter deficits in right putamen/ globus pallidus and corpus striatum.
- Reduced D2/D3 receptors in left caudate nucleus.
- Reduced striatal activation during reward anticipation (compared to increased striatal activation in anxiety patients).

Bipolar Disorder

- Smaller amygdala, reduced volume prefrontal cortex, exaggerated amygdala response to emotional stimuli (Blumberg 2008)
- Grey matter deficits in right anterior cingulate gyrus and ventral striatum.
- White matter volume reduction in left frontal and temperoparietal regions (same frontotemporal disconnectivity as schizophrenia)

Figure 3. Structural brain differences

Structural brain differences

The known structural brain differences are markedly different between ADHD and bipolar disorder [see Figure 3]. Again, similarity exists between bipolar disorder and schizophrenia, as opposed to ADHD.

Cognitive impairment

Being a frontal lobe executive functioning problem, a working memory deficit is a major issue in ADHD. Working memory, particularly spatial working memory, improves with age in ADHD and markedly so in boys. In these boys, visuospatial working memory normalises over time and by adulthood begins to approximate that seen in healthy norms. However, their verbal working memory stays impaired and is not greatly improved by stimulants. Useful learning strategies for these individuals include the use of visualisation, mind-mapping and grouping information to anchor memory and improve recall.

Cognitive impairment is more difficult to determine in bipolar disorder, because for most of the time, an affected individual is symptomatic. It is difficult to know at any point in time how much of the impairment is related to the person's mood state at the time rather than a trait problem related to the bipolar disorder. Nonetheless, the deficit in sustained attention seems to be a trait marker, apparently unrelated to affective symptoms. Notably, this deficit is not observed in remitted unipolar depression or first degree relatives of bipolar disorder.[26]

In addition, some other deficits such as verbal learning and verbal memory worsen as the illness progresses; they correlate with the number of manic episodes and duration of illness. Some dispute whether impaired memory is a state marker sensitive to mania and depression.[27]

Treatment differences

Treatments that work well for ADHD do not work well for bipolar disorder and conversely, all those medications that are normally reserved for bipolar disorder do not work in ADHD. However, selective serotonin reuptake inhibitors (SSRIs) are an anomaly. Many patients who present to private practice, who do not necessarily have co-morbid personality disorder, will have panic attacks, anxiety and depression. Anecdotally, many patients with ADHD feel cognitively worse on SSRI monotherapy, except for sertraline, which is probably the only SSRI that provides a dopaminergic effect as well.

Dr Mastroianni conjectures that the reason patients feel worse cognitively on SSRIs is because they rely on the surge of noradrenaline, the rush of anxiety, to kick in their dopamine and sustain the last-minute pressure to get their act together and focus on non-stimulating activities. SSRIs may block individuals with ADHD from getting into gear as they normally would. However, a combination of stimulants and SSRIs for a co-existing anxiety or mood disorder works well.

Summary

In summary, the onset of ADHD symptoms is before the age of 7 years and can persist into adulthood, whereas the onset of bipolar disorder occurs in over 60% of individuals before age 18 and persists into adulthood. ADHD is predominantly a neurocognitive problem, with or without a behavioural problem, whereas bipolar disorder is predominantly a mood problem that can have behavioural and, over time, neurocognitive problems. The difficulties seen in ADHD are pervasive from childhood, whereas bipolar individuals develop more pervasive problems as time goes on, with marked episodic variations from usual behaviours. In ADHD, inattention improves with age (plateauing by about age 30), and impulsivity and hyperactivity decline with age. Neurocognitive deficits (including attention) deteriorate with age in bipolar disorder and with the longevity/course of illness. If co-morbid behavioural or mood disorders exist in ADHD, the outcome will be worse. In bipolar disorder, the outcome will be worse if there is co-morbid ADHD.

Psychiatrists need to be aware that ADHD can be co-morbid with bipolar disorder and may not merely represent a more severe form of bipolar disorder. Treatment of ADHD (with stimulants or atomoxetine) may be considered after mood stabilisation with treatment of bipolar disorder. Misdiagnosis may cause harm. RANZCP registrar training needs to improve psychiatric skills in the diagnosis and management of ADHD.

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