EARLY DETECTION AND INTERVENTION IN PSYCHOSIS IN AUSTRALIA: HISTORY, PROGRESS AND POTENTIAL

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Abstract

Early intervention for psychosis in Australia has developed from humble beginnings in the early 1980s. Through the energy of key individuals, the movement for reform overcame initial obstacles. However, despite considerable achievement, early intervention is still not mainstream practice in most parts of Australia despite the rhetoric engaged in by government. There have however been successful inroads made into early intervention in non-psychotic disorders based on the advocacy of those in the early psychosis movement. This article describes the history and current situation of early intervention in Australia, as well as pointing to future challenges.

Key Words: Early intervention for psychosis

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Introduction

Australia is an island continent, perhaps best known around the world for its harsh outback regions, its spectacular coastline and beaches, its unique flora and fauna and its laconic and laidback people. However, Australia's researchers have, over the years, made significant contributions in many areas. These include the discovery of how to make penicillin, the use of lithium to treat bipolar disorder, the invention of the bionic ear, the invention of the black box flight recorder, the discovery of the true cause of stomach ulcers and the combine harvester to name but a few. Another area in which Australia has been a leader is in the early detection of and intervention in early psychosis.

Clinical and research endeavours into the early treatment of psychotic illness have existed in Australia since the early 1980s when Patrick McGorry and other colleagues began to focus their attention on comprehensively treating people in the early phase of illness in an effort to reduce disability and potentially prevent progression to more chronic states (McGorry et al. 1996). This early work led to the establishment in 1992 of the Early Psychosis Prevention and Intervention Centre (EPPIC) whose mission was clearly articulated in its name (Killackey and Yung 2007). From this start, and with like minded colleagues around the World (Edwards and McGorry 2002), the early intervention paradigm has grown rapidly from a revolutionary idea in mental health (Killackey et al. 2007) to an accepted part of mainstream service provision in many countries. This article will consider the progress of early detection and intervention in Australia in the quarter century since those first efforts in 1984. It will highlight the current situation of early detection in the Australian context both in the pre-onset and post-onset phases of illness and then will consider some of the challenges that lie ahead.

History

Development of Early Psychosis Services in Australia

As mentioned above, McGorry and colleagues began clinical and research work specifically with people with first episode and recent onset psychosis in

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the early to mid 1980s in the Aubrey Lewis Unit at Royal Park Hospital in Melbourne (McGorry et al. 1996). From their work in this unit they developed an understanding of what elements would be necessary for establishing a fully fledged specialised service for first episode psychosis. Such a unit would require not just a focus on identification, but the development of recovery-focused interventions tailored to this early stage of illness. These interventions would need to include both pharmaceutical and psychosocial elements. A focus specifically on young people was another element. This involved recognition of the importance of the developmental stage of the young person, and the role of the family The lessons learned in the Aubrey Lewis unit paved the way for EPPIC, which began late in 1992.

Given that many now see EPPIC as being the first centre for early intervention in the World (Killackey, Yung 2007) it is interesting to note that McGorry et al. described it as "A second generation model of care" (McGorry et al. 1996). EPPIC was set up as a clinical-research centre where clinical insights would drive research which in turn would lead to improvement in interventions offered. From the outset its model of care was centred on maintaining service users in the community rather than as inpatients. It did this through having a mobile outreach team which was able to offer support to clients and their families in the community. Each client had a case manager who was also their primary therapist. In addition to this there was medical review as well as group programs. The goals of the service were "to address and embrace early detection, to prevent secondary morbidity, and maintain social and occupational functioning during the early'critical period'" (McGorry et al. 1996) (p. 309). It sought to do this through early identification followed by phase specific treatment.

In order to promote early identification of first episode psychosis, an education and knowledge transfer component of EPPIC (which is known as EPPIC Statewide Services, more often referred to as Statewide) was set up. Statewide's mandate was to provide education to key stakeholders about early detection and intervention across the across the state of Victoria. This could include those working at adult and children's mental health services, General Practitioners, school counsellors and anyone else who was likely to come into contact with young people. This strategy ensured that the knowledge that was being generated at EPPIC was disseminated to a wide variety of people. A further knowledge transfer activity in conjunction with The University of Melbourne was the development of a Graduate Diploma in Young People's Mental Health. This course was offered via distance learning and had video taped lectures by key experts on a wide range of topics. This allowed clinicians in all areas of Australia to develop knowledge and skills in this area. Many of the graduates of this course have become leaders for change in their local health services.

Research conducted using this model at EPPIC has shown the ability to reduce the Duration of Untreated Psychosis (DUP) from over a year initially to less than 9 weeks (Schimmelmann et al. 2008). This is important as DUP has been shown to be independently related to outcome (Marshall et al. 2005, Perkins et al. 2005). The results from studies at EPPIC would seem to support this in terms of several outcomes including symptoms, functioning and quality of life (Harris et al. 2005). In addition the early intervention provided at EPPIC has been shown to be an economically valuable intervention. Consistent with findings elsewhere (Access economics), the intervention provided for first episode psychosis at EPPIC has been shown to provide a better value for money intervention than standard care (Mihalopoulos et al. 2007, Mihalopoulos et al. 1999). A recent report by an independent economics firm in Australia found that the potential savings to the health system in Australia if early intervention was routinely available would be AUD$210,000,000 per year (Access Economics 2008). This saving does not include the saving that would also accrue if some of the newer interventions which show great promise such as vocational intervention (iFEVR Group) were also included Killackey et al. 2008).

Impact of Early Psychosis Services in the Australian Context

Initially, the establishment of an early intervention service that cut across traditional service boundaries was met with some resistance (Birleson et al. 2001). However, over time the sense of aligning services with epidemiological data about onset of illness (Vos and Begg 2003), rather than arbitrary division points such as voting age, began to become ascendant. This led the Victorian State Government, which is widely seen in Australia as being a leader in mental health, to mandate the establishment of Youth Early Psychosis Services (YEPS) throughout the Victorian mental health system. In effect this means that in each geographic catchment area in the State of Victoria there are some dedicated early psychosis services. Often this takes the form of one or two workers in an already existing service to whom those with first episode psychosis are referred to for treatment. Although it falls short of an in-depth early psychosis service, it is a positive step in the right direction. This is combined with an increasing focus of government on the health, social and economic benefits of intervening early in their new report discussing the future directions that they will be pursuing (Government of Victoria 2008).

Other states in Australia are also recognising the benefits of early intervention in psychosis. However, progress on the provision of specialist services in these states is variable. The challenges facing some states are both about recognition of the urgency of the problem, and overcoming vast distances and sparse populations to provide services.

Identification and Intervention in the Pre-Onset Phase

Initially, the early psychosis movement focused on timely recognition and phase specific treatment of first episode psychosis. However, it was also recognized that for most patients a prolonged period of non-specific psychiatric symptoms, attenuated psychotic symptoms and impaired functioning precedes the first psychotic

episode (Häfner et al. 1993, Yung et al. 1996). Much of the disability associated with psychotic disorders, particularly schizophrenia, develops long before the onset of frank psychosis and is difficult to reverse even if the first psychotic episode is successfully treated (Häfner et al. 2003). This pre-onset period of illness has been termed the prodromal phase (Yung 2003, Huber et al. 1979). Within the context of the early intervention paradigm, EPPIC researchers suspected that pushing the point of intervention even further back from the first episode of psychosis to the prodromal phase may result in even better outcomes (Yung et al. 1998, McGorry et al. 2001a, McGorry et al. 2001b). Intervening during this phase may ameliorate, delay, or even prevent onset of fully-fledged disorder (Yung 2003), thereby reducing the burden of disability, prevalence, and possibly even the incidence, of psychotic disorders.

One of the main problems with attempting prodromal intervention is the possibility of "false positives"; that is, people who are identified as being possibly prodromal (at risk of developing a psychotic disorder in the near future), but who do not go on to develop the disorder. Those who are in fact not at risk of developing a psychotic disorder (the "true false positives") may be harmed by being labelled "prodromal" or at "high risk of psychosis" and may receive treatment unnecessarily (McGorry et al. 2001b, Bentall and Morrison 2002, Yung and McGorry 1997, Cornblatt et al. 2001, Corcoran et al. 2005). Individuals who would have developed a psychotic disorder, but some alteration in their circumstances (e.g., stress reduction or cessation of illicit drug use) prevented this from occurring have been termed "false false-positives" (Yung et al. 2003). Clearly, it is impossible to distinguish these two groups phenotypically at either baseline or follow-up.

The non-specific nature of the most common prodromal features adds to the likelihood of detecting false positives. Indeed, the term "prodrome" should only be used once the full-blown syndrome has developed (Yung et al. 1996). Prior to diagnosis with a psychotic disorder, the prodrome should be thought of as a risk factor for psychosis, not as a disease entity (i.e., the presence of the syndrome implies that the affected person is at that time more likely to develop psychosis in the near future than someone without the syndrome). However, if the symptoms resolve then this degree of increased risk may remit as well. In an attempt to deal with these issues, we coined a new term - the "ultra high-risk" (UHR) (Yung et al. 2003, Yung et al. 2004) state. In the mid 1990s we developed UHR criteria that attempt to identify individuals with a strong likelihood of developing a psychotic disorder within the near future (e.g., within 12 months).

Due to the non-specific nature of prodromal symptoms, there are problems using these features alone to identify people thought to be at imminent risk of onset of psychotic disorder. Even psychotic-like experiences (attenuated or subthreshold psychotic symptoms) have been found to occur commonly in the general population, especially among adolescents and young adults (Johns et al. 2004, Verdoux and van Os 2002, van Os et al. 2001, Tien 1991). Using symptoms alone would result in a high false-positive rate. Thus, some added criteria were needed to focus on those most likely to be in the prodromal phase of a psychotic disorder. We added the risk factor of age, as the age of highest incidence of psychotic disorder is adolescence and young adulthood (Häfner et al. 1993). Clinical need for care was another factor. Thus, the young person must be seeking help, or be identified by someone, such as a parent or teacher, as needing help. This requirement reduces the chance that a well person who happens to have psychotic-like experiences, but who is otherwise functioning adequately and is not distressed, will be unnecessarily treated for imminent psychosis (Yung et al. 2006a).

We hypothesised that individuals with these multiple risk factors for psychosis would have a high likelihood of developing a psychotic disorder within a short time period. To test this theory, specific operationalised UHR criteria were developed to identify young people at risk for psychotic disorder. The UHR criteria require that a person is aged between 14 and 25, is referred for health care to a psychiatric service, and meets criteria for one or more of the following groups:

Attenuated psychotic symptoms group (APS): patients have experienced subthreshold, attenuated positive psychotic symptoms during the past year;

Brief limited intermittent psychotic symptoms group (BLIPS): patients have experienced episodes of frank psychotic symptoms that have not lasted longer than a week and have spontaneously abated; or

Trait and state risk factor group: patients have schizotypal personality disorder or have a first-degree relative with a psychotic disorder and have experienced a significant decrease in functioning during the previous year.

These criteria are described in more detail elsewhere (Yung et al. 2003, 2004a). To further reduce the risk that well functioning individuals will be identified, since 2006 we have also required that all patients show a significant deterioration in social or occupational functioning (Yung et al. 2006a).

The PACE Clinic

We established a specialised service for the UHR group, the PACE (Personal Assessment and Crisis Evaluation) Clinic, in Melbourne in 1994. This service was the first clinical and research clinic in the world for individuals considered to have incipient psychosis (Yung et al. 1996). Using the UHR criteria, we found a rate of transition to psychosis within 12 months of about 35% (Yung et al. 2003, 2004a), a rate several thousand-fold greater than the expected incidence rate for first-episode psychosis in the general population. This occurred despite the provision of case management and antidepressant medication if required. The primary diagnostic outcome of the group who developed psychosis was schizophrenia (65%). The UHR criteria used in PACE have been adopted, and in some cases adapted, by a number of other centres around the world (Yung et al. 2004b, Olsen and Rosenbaum 2006, Haroun et al. 2006).

The PACE clinic receives referrals of young people seeking help from agencies such as general prac-

titioners, school and university counselling services, community health services and other support agencies for young people, including drug and alcohol services (Phillips et al. 1999). Initially, a case-management model was provided, based around the presenting problems. The added focus of risk and attempted prevention of psychotic disorder was discussed with the patient, but no antipsychotic medication was prescribed (Yung et al. 1996, Yung et al. 2004b). We wanted to determine the "natural history" of the UHR syndromes and to examine the false-positive rate. Subsequently, cognitive behaviour therapy (CBT) and antipsychotic medication have been trialled at PACE. Currently, all clients receive psychoeducation, case management, formulation-based psychotherapy and antidepressant medication if required, (see Yung 2007 and Nelson and Yung 2007, for a detailed account of management of clients at PACE).

The first clinical trial in the UHR group was conducted at PACE from 1996 to 2000 (McGorry et al. 2002). In this trial, the effect of combined CBT plus low-dose antipsychotic (risperidone) medication (treatment group; $n = 31$) was compared with that of supportive therapy (control group; $n = 28$) on the development of a psychotic disorder. At the end of the 6-month treatment phase, significantly more subjects in the control group had developed psychosis than in the treatment group ($P = 0.026$). This difference was no longer significant at the end of a 6-month follow-up period after treatment ($P = 0.16$), although it did remain significant for those members of the treatment group who adhered to the medication regimen. This result suggests that it is possible to delay the onset of a psychotic disorder. Both groups experienced an amelioration of global psychiatric symptoms and improved functioning over the treatment and follow-up phases compared with levels at entry to the study. These results, along with results from intervention trails conducted at other UHR clinics internationally (McGlashan et al. 2004, Morrison et al. 2004), indicate that psychological and psychosocial interventions, either alone or in combination with pharmacotherapy, may be effective in at least delaying, if not preventing, the onset of a psychotic disorder (McGorry et al. 2008). Further research is required to resolve which elements of an intervention are essential at this time point and for how long they need to be applied.

In 1997 the Psychological Assistance Service (PAS) opened in Newcastle, Australia as a clinical service for the assessment and treatment of young people at high risk of psychosis and those experiencing a first psychotic episode. The high-risk criteria are based on those of PACE but also allow inclusion if a young person has a second degree relative with a history of psychotic disorder in conjunction with a significant decline in functioning (Carr et al. 2000). The transition rate to psychosis within a 12-month period was 50% (Mason et al. 2004).

Generalising the early psychosis model to youth mental health

As noted above, our clinical emphasis on the early stages of psychosis through EPPIC and PACE necessarily led to a focus on adolescents and young adults – those in the peak risk period of onset of psychotic illnesses. We developed a growing reputation of having expertise in the area of young peoples' mental health, and in time an opportunity became available through changes in the structure of the Victorian mental health system for EPPIC to expand clinical services to young people with non-psychotic disorders. A new service structure was developed for non-psychotic young people, named "Youthscope". This was a major step forward in increasing the accessibility of psychiatric services to young people. It meant that young people, could present to the expanded clinical service, known as Orygen Youth Health (OYH), with any symptoms of psychological distress, and be assessed for the most appropriate service. This eliminated the difficulty that some families and potential referrers had about not knowing what the "right" service was for a young person. The pressure for general practitioners, counselling services and other organisations to decide whether or not a young person had a psychotic disorder or not was relieved. A central point of referral was established with a single toll free telephone number. A Triage system was established, staffed by experienced clinicians, who could determine the most suitable arm of OYH.

However, one of the problems with this expanded service system was that, due to the high prevalence of non-psychotic disorders in the community (Australian Bureau of Statistics 2008), not all young people who presented could be offered treatment. A study of young people referred to Youthscope found that even among those who were not accepted into the service, there was a high level of psychopathology and functional impairment (Yung et al. 2006b), and that a subgroup of those who were not accepted for treatment, although initially in better condition than those accepted, ended up in worse condition both in terms of symptoms and functioning (Yung, unpublished data) and suicidality (Cosgrave et al. 2007).

As a consequence of this, both of the main political parties in Australia went to the 2004 federal election with a commitment to address the lack of services for youth mental health in Australia. This led to the development in 2005 of the headspace National Youth Mental Health Initiative. This service, when fully rolled out will be a primary health service for the mental health needs of young Australians aged 12 to 25 years.

At around the same time, data from the PACE clinic was increasingly indicating that people who are UHR for psychosis commonly present with a range of threshold and subthreshold non-psychotic disorders, including depression. Many UHR patients were also shown to develop non-psychotic disorders rather than transition to psychotic disorder.

These two factors: our increasing experience with young people with non-psychotic disorders, and the finding of non-specific risk factors for the onset range of mental disorders, including psychotic and psychotic illnesses, led to the formulation of the clinical staging model (McGorry et al. 2006).

The Clinical Staging Model

Clinical staging is a deceptively simple and practical tool that is useful in other areas of medicine, such as oncology. Clinical staging differs from conventional diagnostic practice in that it defines the extent of progression of disease at a particular point in time, and where a person lies currently along the continuum of the course of illness. The differentiation of early and milder clinical phenomena from those that accompany illness extension, progression and chronicity lies at the heart of the concept. Put simply, the hypothesis is that severe mental disorders (including substance use disorders) develop from initial non-specific symptoms and syndromes, from a background of specific and non-specific risk factors (e.g. genes, early environment). From the initial non-specific or pluripotential clinical picture, worsening of symptoms and acquisition of new symptoms occurs, together with progressive neurobiological abnormalities and related neurobehavioural deficits, until clear-cut recognizable mental disorders appear. Progression of symptoms and neurobiological abnormalities may continue after "threshold" diagnosis. Thus, the natural history of major mental illnesses such as psychotic and mood disorders, is theorized to consist of transition from being asymptomatic and non-help-seeking, through a stage of undifferentiated general symptoms such as mild anxiety, depressive and somatic symptoms, then worsening of existing symptoms and acquisition of new ones, which may include psychotic-like experiences and substance use problems, and may be associated with behavioural and functional decline. This pattern continues until a "threshold diagnosis" is reached (such as major depression or schizophreniform disorder). After such diagnosis, progression of illness may still occur, with development of chronic symptoms, frequent relapses and ongoing functional decline.

It is important to note that transition from one stage to the next is by no means inevitable. For example, a person with mild anxiety and depressive symptoms may not progress to develop more severe symptoms and may not seek help. A person with moderate depression, psychotic-like experiences, and some functional deterioration may not develop a mood or psychotic disorder. A person with a first episode of psychosis (diagnosed as having schizophreniform disorder) may not relapse or progress to a chronic deteriorating course. Thus there are a number of possible trajectories at any one time.

The reason for non-transition may be that the person was never "destined" to progress from one stage to the next. That is, although he or she was phenotypically indistinguishable from someone who did progress to the next stage, in fact these two people had different underlying disorders. If this were the case, then they would be expected to have different underlying "trait markers" or "risk indicators". For example, they might have different genes, neurobiology or early environmental influences. Alternatively a person might not make the transition from one stage to the next because he or she was prevented from doing so by some intervention or other protective (resilience) factors. For example, some peer support may prevent a young person with mild depressive symptoms from developing more severe symptoms and dropping out of school. Cognitive behaviour therapy may prevent someone with psychotic-like experiences and functional decline from developing a first episode of psychosis. Thus these people who *would have* progressed from one stage to the next, but did not (the false false positive idea, discussed above), should share trait markers with those who do make the transition (for example have the same gene markers, brain structure etc).

This novel way of thinking about onset and progression of serious mental illnesses is particularly applicable to young people in adolescence and young adulthood, as this is the period of maximum risk of onset of severe mood, anxiety, psychotic and substance use disorders.

One of the implications of thinking about mental disorders in this way is that it guides the search for risk factors for transition. As described above, these risk factors could be underlying risk indicators or trait markers, such as genetic markers, brain abnormalities, abnormal early environment and so on. The benefit in identifying these markers is that we may be able to differentiate between types of disorder. That is, we may ultimately identify a "neurodevelopmental schizophrenia" characterised by a certain genotype, brain structural and cognitive deficits, or a severe depressive disorder similarly characterised by failure to respond to simple interventions and other trait markers, or we may be able to detect bipolar disorder before the advent of any manic syndrome. One of the challenges in being able to do this will be the ability to identify these risk indicators and to distinguish them from state markers, which will vary depending on current mental state and where someone lies on the continuum of progression of illness.

The other advantage of the staging model is that it provides a heuristic framework for the testing of preventively oriented treatments. For example, some state markers may be identified that are potentially mutable and thus the degree of risk of transition to the next stage may be modifiable. An example is that cognitive deficits in major depression may improve with cognitive remediation. Perceived stress and its biological correlates such as high cortisol level and hypothalamic-pituitary axis changes, including increased pituitary size (Garner et al. 2005), which act as risk factors and state markers for transition across a number of stages, may be reduced by cognitive therapy, exercise and/or anti-depressant medication. An important implication is that treatments should be benign, non-specific and cost effective in the early stages. If progression occurs, more specific and expensive treatments, that often have more side effects, such as anti-psychotic medications or mood stabilisers, may be required. That is, less differentiated early phases of mental illnesses may benefit from broad-spectrum simpler treatments, saving more costly and possibly toxic interventions for more differentiated later illness stages in people unresponsive to the more benign treatments. This could enable young people to receive the help they need in a timely manner, with the potential for less suffering and improved outcomes.

Conclusion

Early intervention in psychosis in Australia

continues to develop. After a quarter of a century of development, the maverick area of psychiatry is beginning to become part of the mainstream. However, development into the mainstream is still dependent on the fierce advocacy of a chorus of clinicians, service users and researchers. Pleasingly, the application of the hard learned lessons of early intervention in psychosis are beginning to be adapted and applied to the high prevalence disorders. Partially this is an acknowledgment of their higher prevalence, but also an acceptance of the reality that the pathway to psychosis often passes through these syndromes first.

While it would be easy to congratulate ourselves on what has been achieved, it is important that the energy that has characterised the first 25 years does not dissipate for there is still much to do. Early intervention is acknowledged best practice but has not been implemented throughout the country. Recent data shows that people who experience an episode of psychosis still have worse functional and social outcomes than they should. The gap between what we know works and what is applied has not been comprehensively closed. It is important that the case for reform, backed by the increasing amount of local and international knowledge, continues to be put.

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