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Psychotic Prodrome



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18 February 2014

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Disclosure to Audience

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- **“The best hope now for the prevention of schizophrenia lies with indicated preventive interventions targeted at individuals manifesting precursor signs and symptoms who have not yet met full criteria for diagnosis. The identification of individuals at this early stage, coupled with the introduction of pharmacological and psychosocial interventions, may prevent the development of the full-blown disorder”.**

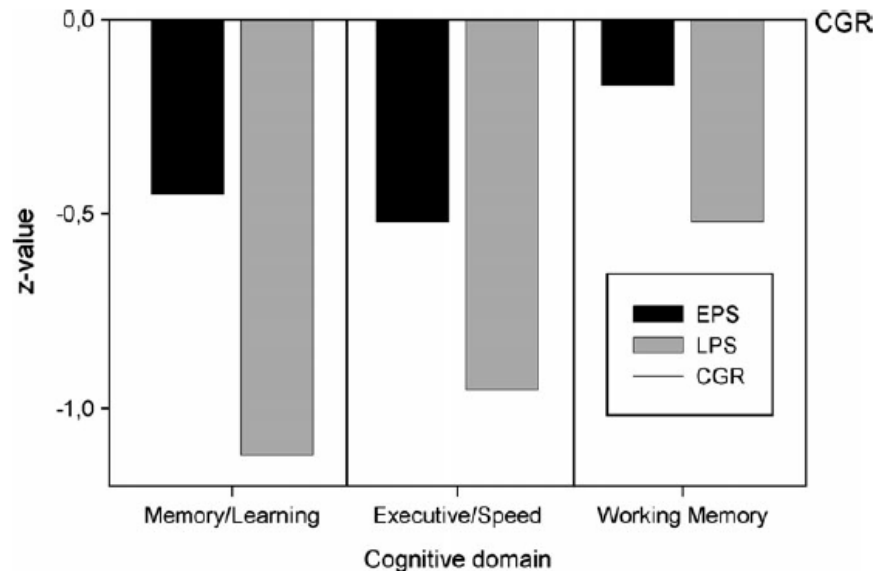
**-taken from 1994 book entitled
*Reducing Risks for Mental Disorders:
Frontiers for Preventive Intervention
Research***



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Neuropsychology of Psychotic Prodrome

- Cognitive deficits have been noted as a core feature of schizophrenia since at least Kraepelin's early descriptions
 - These deficits have been documented in early stages of the disease to very early in first-episode psychosis
 - Less well documented in peer-reviewed literature is cognitive functioning during the prodromal stage of the disease





Neuropsychology of Psychotic Prodrome

- Cognitive deficits often persist despite relatively successful pharmacotherapy
 - Cognitive deficits are not significantly associated with clinical symptoms
 - Bilder et al. (2000): found no correlation between positive symptoms and cognitive dysfunction; negative symptoms correlated mildly

TABLE 3. Correlations Between Clinical Variables and Neuropsychological Scale Scores Among 94 Patients With First-Episode Schizophrenia

Variable	Correlation With Neuropsychological Scale Score (r, two-tailed)							
	Language	Memory	Attention	Executive	Motor	Visuospatial	Premorbid Functioning	Global
Scale for the Assessment of Negative Symptoms								
Affective flattening	-0.21	-0.27	-0.30*	-0.39**	-0.27	-0.34	-0.16	-0.38*†
Alogia	-0.16	-0.34**	-0.34**	-0.41**	-0.23	-0.32*	-0.16	-0.37**
Apathy	-0.09	-0.08	-0.26	-0.30*	-0.34**	0.35**	0.00	-0.31*
Anhedonia	-0.05	-0.22	-0.23	-0.28	-0.33*	-0.23	-0.05	-0.28
Attention impairment	-0.19	-0.30	-0.27	-0.30*	-0.19	-0.13	-0.18	-0.26



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Neuropsychology of Psychotic Prodrome

- **Cognitive deficits are often the source of significant functional impairment in successfully treated schizophrenia**
 - **Contribute to significantly decreased QOL and reduced social support**
 - **Contribute to difficulty maintaining engagement with helping agencies**
 - **Decrease problem solving skills and ability to engage in psychosocial interventions**



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Neuropsychology of Psychotic Prodrome

- Premorbid and prodromal personality characteristics load in predictable fashion amongst at-risk patients
 - Cluster A (schizotypal is most predictive: ~25% go on to be diagnosed with schizophrenia)
 - No specific demographic or psychopathological variables differentially predicted psychosis (i.e. schizotypal PD may differ from schizophrenia only as a sub-psychotic form of the same condition)

Table 3. Cox Proportional Hazard Model

Predictor Variable	β	SE	Wald,	HR (95% CI)	P Value
SIPS Positive subscale score >16	1.571	0.428	13.46	4.81 (2.078-11.134)	<.001
Bizarre thinking score >2 on SIPS	0.865	0.387	4.99	2.38 (1.112-5.074)	.03
Sleep disturbances score >2 on SIPS	0.793	0.387	4.19	2.21 (1.034-4.717)	.04
Schizotypal personality disorder according to SIPS	1.037	0.423	6.01	2.82 (1.231-6.464)	.01
GAF-M score, highest in the past year ^a	0.033	0.015	5.02	1.03 (1.004-1.064)	.03
Years of education, including university ^a	0.250	0.086	8.35	1.28 (1.084-1.521)	.004



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Neuropsychology of Psychotic Prodrome

- Premorbid and prodromal personality characteristics load in predictable fashion amongst at-risk patients
 - Cluster C (Avoidant is most predictive)
 - Cluster B (Predictive of non-psychotic severe psychopathology)



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Demographics

- **25 year-old, single Caucasian male**

- **ADAF, E-3**
 - **Three years in military**
 - **Comm technician (radar maintenance)**

- **Originally from Virginia and Rhode Island**

- **JBER-Elmendorf is first duty station**



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Commander Directed Evaluation

- **Commander requested CDE due to odd behaviors**
 - Smashing his personal computer “because it made him angry” discovered by his 1st Sergeant after he failed to return to work after lunch (21Nov12)
 - Sitting in sub-freezing temperatures on his dorm balcony in the fetal position unresponsive to questioning from concerned peers on adjacent balcony (01Dec12)
 - Found walking around during a snowstorm and entering a building on base and appearing disoriented when questioned on his reasons for being there when discovered (15Dec12)

- **CDE conducted 15Jan13 by Capt Kerst**



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History

- **Parents are still married (pt and them are close) and pt has 1 sister**
 - **Home-schooled through high school graduation**
 - **History of one episode of sexual abuse by an older male babysitter when he was 5**
 - **Denies memories of this event; parents knew and acted immediately to discontinue contact**
 - **Identifies as Christian currently; raised in Seventh Day Adventist church**
 - **Identifies as heterosexual; no reported prior relationships**
-



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History

- **Involved in a local church but reported no significant social contact outside of acquaintances at work**
- **Identified by co-workers as “odd”, “quiet”, and a “loner” but a smart technician making good progress on upgrade training**
- **Family History**
 - **No reported family history of significant mental health concerns, substance use/abuse, or significant medical problems**



Personal Medical History

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- **Treated by GI doctor and his mother for candidiasis as a child**
- **Childhood history of mumps with biopsy**
- **History of childhood asthma which resolved in adulthood**
- **Unremarkable adult medical history**
- **Not currently on any medications**



Clinical Interview: 15Jan

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- **Presented as very anxious and unsure of his responses throughout interview.**
- **Poor eye contact**
- **Long latency to respond to questions**
- **Refused to elucidate on motivations for bizarre behavior**
- **Reluctantly acknowledged that his behaviors could be seen as odd but noted that they were not “too far from normal”**
- **Did not endorse significant mood, mania, anxiety, or psychotic symptoms on unstructured interview**



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Clinical Interview: 15Jan Assessments

- **Outcome Questionnaire – 45: 54 (non-clinical self-reported functional problems in all domains)**
- **MINI 6.0 (structured clinical interview for diagnosis of most major Axis I)**
 - **Endorsed significant symptoms for Social Phobia; denied all others**

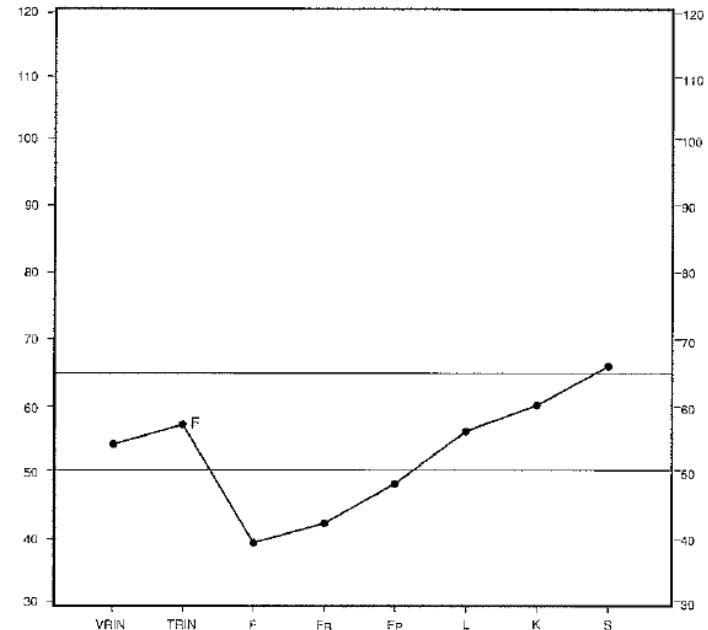


Clinical Interview: 15Jan Assessments

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- **MMPI-2 (consistent and valid but defensive)**
 - **No significant elevations on clinical scales**
 - **Content scale elevations: SOD - 71**
 - **Uncomfortable in social situations, trouble trusting others, trouble forming close relationships, but with fair insight that his social functioning is poor**

MMPI-2 VALIDITY PATTERN



Raw Score:	6	8	1	0	1	5	20	39
T Score:	54	57F	39	42	48	56	60	66
Response %:	100	100	100	100	100	100	100	100

Cannot Say (Raw): 0
 Percent True: 30
 Percent False: 70

	Raw Score	T Score	Resp. %
S1 - Beliefs in Human Goodness	15	70	100
S2 - Serenity	7	53	100
S3 - Contentment with Life	8	60	100
S4 - Patience/Denial of Irritability	7	63	100
S5 - Denial of Moral Flaws	4	58	100



Clinical Interview: 15Jan Assessments

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- **MCMI-III (consistent and valid but defensive)**
 - **Defensive**
 - **Severe Personality Pathology: Schizotypal- 75**
 - **Personality code: 17 2A (Schizoid: 78, Compulsive: 68, Avoidant: 62)**
 - **Prone to unusual beliefs/experiences; little interest in social activities, emotionally constrained, interpersonally distant.**

INVALIDITY (SCALE V) = 0 INCONSISTENCY (SCALE W) = 1
 PERSONALITY CODE: - ** 1 * 7 2A + 5 3 4 " 6A 2B 6B 8A 8B ' // - ** S * //
 SYNDROME CODE: - ** - * // - ** - * //
 DEMOGRAPHIC CODE: 038700038/ON/M/24/W/N/13/OT/--/-----/---/-----/

CATEGORY	SCORE	PROFILE OF BR SCORES				DIAGNOSTIC SCALES			
		RAW	BR	0	60		75	85	115
MODIFYING INDICES	X	48	8						DISCLOSURE
	Y	11	51						DESIRABILITY
	Z	1	18						DEBASEMENT
CLINICAL PERSONALITY PATTERNS	1	7	78						SCHIZOID
	2A	4	62						AVOIDANT
	2B	0	14						DEPRESSIVE
	3	3	44						DEPENDENT
	4	7	42						HISTRIONIC
	5	9	58						NARCISSISTIC
	6A	1	26						ANTISOCIAL
	6B	0	14						SADISTIC
	7	15	68						COMPULSIVE
SEVERE PERSONALITY PATHOLOGY	8A	0	14						NEGATIVISTIC
	8B	0	14						MASOCHISTIC
	S	7	75						SCHIZOTYPAL
CLINICAL SYNDROMES	C	0	8						BORDERLINE
	P	0	8						PARANOID
	A	0	8						ANXIETY
SEVERE CLINICAL SYNDROMES	H	0	8						SOMATIFORM
	N	5	68						BIPOLAR: MANIC
	D	0	8						DYSTHYMIA
	B	0	8						ALCOHOL DEPENDENCE
	T	0	8						DRUG DEPENDENCE
	R	0	8						POST-TRAUMATIC STRESS
SEVERE CLINICAL SYNDROMES	SS	2	38						THOUGHT DISORDER
	CC	0	8						MAJOR DEPRESSION
	PP	0	8						DELUSIONAL DISORDER



Clinical Assessment: 29Jan

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- **Concerns regarding cognition prompted further assessment**
 - **WAIS-IV and CPT**

- **Female psychometrician**
 - **Later learn that he is “afraid” of women and this may have impacted testing**

- **Patient referred to psychiatry for additional clinical interview**
11Feb

- **Collateral interview with sister reveals family concerns as well**

- **Referred for brain MRI to rule out organic causes (read as WNL)**
 - **Patient noted to be “very strange” by radiology staff**



Clinical Assessment: 29Jan

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- **WAIS-IV administration was largely normal with concerns noted in areas of attention and processing speed**

WAIS-IV (29Jan13)	Raw Score	Scaled Score	%ile
Similarities	30	13	84
Vocabulary	41	12	75
Information	21	15	95
VCI	118		88
Block Design	48	10	50
Matrix Reasoning	22	13	84
Visual Puzzles	16	10	50
PRI	105		63
Digit Span	29	10	50
Arithmetic	10	7	16
WMI	92		30
Symbol Search	30	9	37
Coding	45	5	5
PSI	84		14
FSIQ	102		55
GAI	113		81

Conners' CPT II (29Jan13)	Confidence Index
Clinical	60.69
Non-Clinical	39.31



Clinical Assessment: 11Feb

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- **Psychiatric interview**
 - **History obtained was consistent with information gathered by CPT Kerst**
 - **Notable mental status findings included prominent psychomotor restlessness, a guarded attitude during the interview, prominent anxiety that did not decrease as interview progressed, mild loosening of thoughts and increased latency of responses to questions.**
 - **Patient continued to state that some of his behaviors could appear odd to other people but asserted that they were “not that different from normal”**
 - **He denied mood, anxiety, manic or psychotic symptoms**



Treatment Recommendations

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- **Patient was encouraged to engage in treatment in the mental health clinic (either for therapy, medication or both) but declined**
- **Patient did not meet involuntary hospitalization criteria**
- **Feedback was provided to both patient and his command regarding concern about possible development of more severe psychotic symptoms**



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Schizotypal Personality Disorder

- A pervasive pattern of social and interpersonal deficits marked by acute discomfort with, and reduced capacity for, close relationships as well as by cognitive or perceptual distortions and eccentricities of behavior, beginning by early adulthood and present in a variety of contexts, as indicated by 5 or more of the following:
 - 1) ideas of reference (Note: NOT delusions of reference)
 - 2) odd beliefs or magical thinking that influences behavior and is inconsistent with subcultural norms
 - 3) unusual perceptual experiences, including bodily illusions
 - 4) *odd thinking and speech*
 - 5) *suspiciousness or paranoid ideation*
 - 6) *inappropriate or constricted affect*
 - 7) *behavior or appearance that is odd, eccentric or peculiar*



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- **8) *lack of close friends or confidants other than first degree relatives***
- **9) *excessive social anxiety that does not diminish with familiarity and tends to be associated with paranoid fears rather than negative judgments about self***

- **NOTE: If criteria are met prior to the onset of schizophrenia, add “premorbid”**



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Prodrome

- **Webster's Dictionary:** An early symptom indicating the onset of a disorder

- **NIMH:** Period preceding the onset of the first florid psychotic episode, when there is increasing symptomatic presentation and functional deterioration



Psychotic Prodrome

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- **Common Symptoms:**
 - **Anxiety/Restlessness**
 - **Impulsivity**
 - **Suicidal ideas**
 - **Mood swings**
 - ***Apathy***
 - ***Disturbance of attention and concentration***
 - ***Preoccupation/Daydreaming***
 - ***Gradual worsening of perceptual disturbance***
 - ***Referential thinking***
 - ***Paranoia (short of delusions)***
 - ***Cognitive deficits***



Prodrome Significance

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- **Retrospective study in 1996 demonstrated that 21/21 patients with diagnosis of schizophrenia had experienced a prodrome (range in duration from 3 days to 6 years)**

Prospective study in 2001 revealed that 77/79 (98%) of patients who had developed schizophrenia within 10 years of initial appointment met prodrome criteria at initial intake.

Overall estimated rate of progression from prodrome to “full psychosis” is between 10% and 50%. (Prodrome is bit of misnomer)

Take Home Message: The majority of people with schizophrenia have experienced a prodrome, but only a relatively small percentage of people with prodrome may progress to fully psychosis.



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- **Potential Benefits of Recognizing/Treating Prodrome**
 - **Easier to engage patient at pre-psychotic stage**
 - **Minimize common comorbidities that develop with untreated psychosis**
 - **Prevention, or even just delay, of psychosis onset can allow time for important milestones to be reached**



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Ultra High-Risk Criteria ("At-Risk Mental State")

- **State and trait risk factors:**
 - **1) First degree relative with any history of psychotic disorder or bipolar disorder or schizotypal personality disorder AND**
 - **2) Reduction on GAF scale of 30% or more (or clear decline in functional level)**

Attenuated psychotic symptoms:

- 1) At least one of these symptoms: ideas of reference, odd beliefs or magical thinking, perceptual disturbance, digressive speech or thought, odd behavior or appearance AND**
- 2) Symptoms occur at least several times per week AND**
- 3) The change in mental state has been present for at least one week**



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- **Transient psychotic symptoms:**
 - **1) At least one of: perceptual disturbance or hallucinations, delusions of reference, formal thought disorder symptoms AND 2) Duration of symptoms is less than one week and resolves spontaneously**



Clinical Assessment: 12Mar

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RBANS (12Mar13)	Raw Score	Index/T-Score	%ile
Immediate Memory		78	7
List Learning	22	Z= -2.02	2
Story Memory	17	Z= -0.64	25
Visuospatial/Constructional		72	3
Figure Copy	14	Z= -3.92	0.01
Line Orientation	18	Z= 0.40	63
Language		96	40
Picture Naming	10	Z= 0.57	70
Semantic Fluency	20	Z= -0.43	32
Attention		64	1
Digit Span	8	Z= -1.48	7
Coding	38	Z= -2.10	2
Delayed Memory		85	16
List Recall	8	Z= 0.28	61
List Recognition	19	Z= -1.14	13
Story Recall	10	Z= -0.05	47
Figure Recall	8	Z= -2.79	0.26
Total Scale		74	4

Symbol-Digit Modalities Test (12Mar13)	Raw Score	Z Score	%ile
Written	41	-1.9	3
Oral	52	-1.2	12

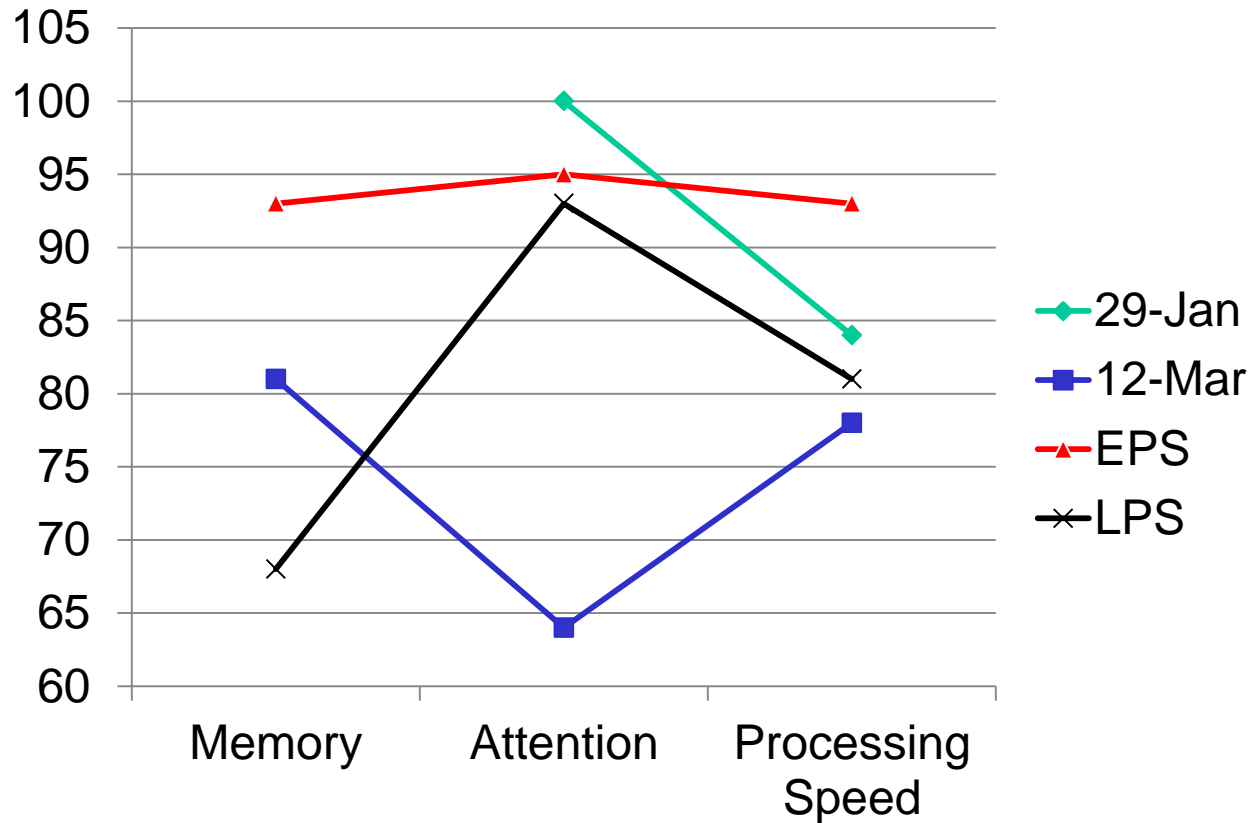
D-KEFS (12Mar13)		Raw Score	Scaled Score	%ile
Trails:	Condition 1	25	9	37
	Condition 2	31	10	50
	Condition 3	50	4	2
	Condition 4	56	11	63
	Condition 5	28	11	63
Composite: Number + Letter		14	7	16
Verbal Fluency:				
Letter Total		37	10	50
Category Total		23	4	2
Category Switching Total		9	4	2
Category Switching Accuracy		8	6	9
Color-Word Interference:				
Condition 1 – Color Naming		30	9	37
Condition 2 – Word Reading		22	10	50
Condition 3 – Inhibition		53	9	37
Condition 4 – Inhib./Switching		70	7	16

Halstead-Reitan Battery (12Mar13)		Raw Score	T Score	%ile
Category Test	Regular	Errors: 34	45	30
	Subtest I	1		
	Subtest II	2		
	Subtest III	11		
	Subtest IV	5		
	Subtest V	6		
	Subtest VI	8		
	Subtest VII	1		



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Clinical Assessment: Comparisons



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Feedback to Commander

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■ **Diagnoses**

- **Axis I: Psychotic Disorder NOS; Rule Out: Schizophrenia prodrome**
- **Axis II: Rule Out: Schizotypal Personality Disorder (Primary Diagnosis)**
- **Axis III: None-contributory**
- **Axis IV: Geographical separation from social support, stressful work environment**
- **Axis V: GAF (Current) 60**

■ **Recommendations**

- **Unfit for military service and needs an MEB**
- **Not currently reliable to hold a security clearance.**
- **Not imminently dangerous but does not have clearance to bear firearms.**
- **Needs evaluation by a psychiatrist to determine need for psychotherapy or pharmacotherapy.**
- **Continue to be engaged with his family and his church and participate in volunteer activities to maintain social engagement and bolster coping strategies.**

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Feedback to Patient

- **Appears unconcerned with diagnosis**
- **Refuses recommendation for evaluation and treatment**
- **Assents to MEB which is submitted**
- **Patient participates in MEB briefing on DoD side**
- **Patient refuses VA evaluation which causes problems with processing the MEB**
 - **Questions about capacity to understand ramifications**



Emergency CDE: 01 May

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- **Commander requests E-CDE due to concerning behavior**
 - **Refused to take out ear plugs at work and off-duty**
 - **Seen wearing glasses with periphery taped to limit field of vision while driving**
 - **Drove through red light while in GOV with a passenger and appeared “out of it” and did not respond to the passenger when implored to stop**
 - **Increasingly socially withdrawn, unproductive at work, refuses to answer questions about his behavior from 1st Sgt and Commander**



Emergency CDE: 01 May

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■ Clinical interview in ER

- Increased latency of responses compared to first assessments (Jan)
- Even less speech compared to first assessments
- When pressed on thought content acknowledges obsessive sexual thoughts, associations between benign stimuli and sexual thoughts (this is why he wears ear plugs and taped his glasses – to limit these stimuli), and anxiety related to these intrusive thoughts.
- Refuses further evaluation and treatment including voluntary hospitalization

■ Assessment

- SANS: $z = 1.36$ (compared to sample diagnosed with schizophrenia)
- SAPS: $z = 0.09$ (compared to sample diagnosed with schizophrenia)

■ Recommendations to Commander

- Limit driving privileges since he refuses to remove glasses/ear plugs
- Not imminently dangerous or gravely impaired at this time



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Mental Health Treatment Team

Meeting: 31 May

- **Meeting with patient, Commander, Shirt, supervisor, Capt Kerst, and Maj Alcorn**
- **Patient is seen in waiting room standing off to the side, rocking back and forth slightly, and tapping his ear plugs with his fingers**
- **During meeting all present discuss concerns with his behavior and duty performance**
- **Patient is largely unresponsive unless directly pressed for input and continues to refuse treatment despite clear discussion of his diagnosis and the risks of refusing treatment**



Emergency Eval in ER: 30Jun

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- **Patient found wandering on back side of base by SF**
- **Had trash bag with chemicals, tubes, and a knife**
- **Patient had been breaking into an old Comm building and rummaging**
- **Pt reported that he was building a cow stomach because people don't eat as they should**
- **Pt's dorm room searched and evidence found that he has been collecting grass and bark and attempting to cook or ferment it presumably for consumption**
- **Pt refuses to answer questions on motivations besides that he is trying build a cow stomach**
- **Photos of a woman he knows are found as his computer desktop**
- **Hairs he has collected are found in envelopes with notes on where he found them, reminders to stitch them into the crotch of his underwear, and questions about whether or not this hair is from a specific woman**

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Emergency Eval in ER: 30Jun

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- **Patient involuntary admitted to API for psychotic symptoms and grave disability**
- **Patient started on olanzapine after refusing medications and a medication order being issued**
- **Patient shows minimal improvement over course of 30 day commitment**



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Currently

- **Upon discharge from API pt is sent for inpatient treatment at Brockton VAMC to be nearer his family for support**
- **Pt shows minimal improvement over course of care at Brockton VAMC but is ultimately discharged after 2 weeks**
- **Pt is placed on convalescent leave until his terminal leave begins since MEB decision is for medical retirement**
- **Pt has shown minimal improvement to date and limited engagement in outpatient treatment with psychiatric provider**
- **Pt refuses to engage in outpatient day program**

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Prodrome Treatment

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- **11 randomized controlled studies have been performed looking at various treatment modalities (eg, antipsychotics, CBT, Omega 3 Fatty acids, antidepressants)**

Findings:

1) Risperidone, Abilify and amisulpride have been shown to reduce conversion to psychosis; Olanzapine did not show statistical significance

2) High doses of antipsychotics were not more successful than lower doses of antipsychotics and increased side effects

3) Strong effect sizes were shown for CBT (or cognitive enhancement therapy), Omega 3 Fatty acids and combined psychosocial treatment



Omega 3 Fatty Acids

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- **Theory: decrease free radicals, increase antioxidants, reduce cellular injury and provide membrane enhancement**

- **Study:**
 - **3 month study using doses of 1200 mg**
 - **Overall progression rate to psychosis was 27.5% in control group vs. 4.9% in treatment group**
 - **NNT was 4 (compared to NNT of 14 for ASA in stroke patients)**
 - **Small sample size, repeat studies are needed**



CBT

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- **Reduce persistent positive symptoms**
- **Increase adaptation to illness**
- **Reduce comorbid substance use**

- **Study: 40 hours of cognitive and social cognitive training provided over 8 weeks**
 - **Increased processing speed**
 - **Increased visual learning ability**



Guiding Principles

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- **CHR (Ultra High Risk) is not that uncommon; don't be surprised and do not overreact to it**
- **Psychosis is on a continuum.**
- **Depression and anxiety are to be expected – Treat what you see.**
- **Marijuana is a contributing risk factor for development of full psychosis. Aggressively treat substance use.**
- **Childhood trauma impacts course of psychosis development; do not automatically assume it is PTSD.**
- **Be vigilant of cognitive decline.**



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Australian Clinical Guideline for Prodrome Treatment

- **Omega 3 FAs may prevent or delay transition to psychosis**
- **Psychological and/or pharmacological treatment or comorbidities should receive priority over targeting attenuated psychotic phenomena**
- **Antipsychotic medication should NOT be considered as a first line treatment for psychotic prodrome**
- **CBT and/or supportive counseling can prevent or delay transition to psychosis during the prodrome and improve overall social functioning**



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“The onset of a mental illness is generally a gradual one; for rarely, the disorder befalls the human all of the sudden without any precursors.”

-Kraepelin, 1909

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“Statistics are that one out of every four Americans is suffering from some form of mental illness. Think of your three best friends. If they are okay, then it’s you...”

-Rita Mae Brown

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Thank you

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NORTH STAR BHS - CME ACTIVITY COURSE EVALUATION FORM

Date: 02/18/2014

Starting Time: 12:00 pm

Ending Time: 1:00 pm

Topic: **Psychotic Prodrome: A Case Study Examining the Evolving Nature of Psychotic Illness**

Presenter(s): **Michael Alcorn, MD and William Kerst, PhD**

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At the conclusion of this activity, participants should be able to:	Not at All	Slightly	Moderately	Mostly	Completely
At the completion of this program, the learner will be able to describe the evolving course of the behavioral, psychological, and cognitive signs and symptoms of the psychotic prodrome.					
By the end of this program, participants will be able to better assess the risk of development of psychotic disorders in adolescents and young adults in at-risk-mental-states.					
Upon completing this program, learners will demonstrate increased competence in choosing and applying up-to-date evidence-based pharmacological, behavioral, and cognitive interventions for the treatment of presumptive psychotic prodrome in adolescents and young adults.					

Was the presentation commercially biased in any manner? Yes No

Based on your participation, will you change anything in your practice? Yes No

Based on this activity, what will you do differently in your practice? _____

Topics of Interest for future Seminars: _____

Printed Name of CME participant: _____ Physician Yes No

Signature of CME participant: _____

Agency/Organization: _____

Email: _____

Are you on our email distribution list? Yes No

If not – do you wish to be added for future CME events? Yes No