2013 Webinar Series

State of the Science:

Dementia Evaluation and Management among Diverse Older Adults and their Families

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Stanford Geriatric Education Center

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State of the Science:

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Sponsored by Stanford Geriatric Education Center in conjunction with American Geriatrics Society, California Area Health Education Centers, & Community Health Partnership

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Cultural Aspects of the Pharmacological Management of Dementia

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STANFORD UNIVERSITY

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Q & A after the presentation

- We will reserve time at the end of the presentation for questions. if you have any questions, please use the "Chat" feature located on the right side of your screen. **Please send your chat to everyone if possible.**
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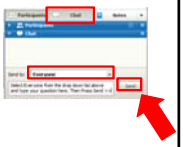

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State of the Science:
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2013 WEBINAR SERIES

"Cultural Aspects of the Pharmacological Management of Dementia"

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About the Presenter

Rita Hargrave M.D., F.AP.A.

Rita Hargrave M.D. is geriatric psychiatrist at the Veteran's Administration Martinez Outpatient Mental Health Clinic and consulting psychiatrist for the University of California , Davis Alzheimer's Disease Center. She is an instructor at the University of California, Davis Department of Psychiatry.

She serves as the Chair of the ABPN Committee for Certification and Recertification in Geriatric Psychiatry. She is a member of the core faculty of the Stanford Geriatric Education Center. For many years she has been a prolific contributor to journals, magazines and books exploring neuropsychiatry, cross-cultural psychiatry and ethnic minority caregivers.

She founded www.ethnicelderscare.net, a website focused on ethnicity and dementia.

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CULTURAL ASPECTS OF THE PHARMACOLOGICAL MANAGEMENT OF DEMENTIA

KEY-POINTS

There are genetic and biological factors that affect the efficacy of the pharmacological management of dementia

There psychological and social factors that affect the efficacy of the pharmacological management of dementia

KEEP YOUR EYES AND EARS OPEN

BE PATIENT

CULTURAL ASPECTS OF THE PHARMACOLOGICAL MANAGEMENT OF DEMENTIA

"The prescription and use of medication fundamentally involves a social transaction that carries both symbolic and social meanings based on the interactions between the patient, doctor and their social environment"

Moerman, D.E.(1979) Anthropology of Healing. Curr.Anthropology, 20. 59-80

CULTURAL ASPECTS OF THE PHARMACOLOGICAL MANAGEMENT OF DEMENTIA

- Majority of studies done in the 1970-1980's without current gene mapping technology
- Older adults were not included in these studies
- Sample size of participants was often small (<20)

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OUTLINE

- Genetic Factors
  - Drug Metabolizing Enzymes
  - Antidepressant Ethnic Differences
  - Antipsychotic Ethnic Differences
  - Benzodiazepine Ethnic Differences
  - Cognitive Enhancer Ethnic Differences
- Non-Genetic Factors
  - Cultural Formulation Interview
  - Cultural and Attitudes to Medications
  - Diet and Habits
  - Alternative Health Practices

CULTURAL ASPECTS OF THE PHARMACOLOGICAL MANAGEMENT OF DEMENTIA

- **Genetic Factors**
  - **Drug Metabolizing Enzymes**
  - Antidepressant Ethnic Differences
  - Antipsychotic Ethnic Differences
  - Benzodiazepine Ethnic Differences
  - Cognitive Enhancers Differences

DRUG METABOLIZING ENZYMES

- Enzymes most studied are the Cytochrome P450 group
  - More than 20 isoenzymes each encoded with a different gene
  - Key component in the oxidation of numerous psychopharmacological agents
- Most drug metabolism involves CYP1, CYP2, CYP3
- Inter-individual and inter-ethnic differences can range from 5 fold in CYP3A4 to 20 fold for CYP2D6

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DRUG METABOLIZING ENZYMES

- Metabolic Subgroups
  - Utra-rapid Metabolizer (UM)
  - Normal or Extensive metabolizer (EM)
  - Intermediate Metabolizer (IM)
  - Poor Metabolizer (PM)

% of POOR METABOLIZERS by ethnicity and enzyme

Enzyme	Ethnicity	% Poor Metabolizers
CYP 2C19 (8 polymorphisms)	Asian Black White	15-30 2-4 3-5
CYP 2D6 (> 100 polymorphisms	White Black Asian Arab	5-10 3 1-2 1
CYP 2C9	White Black Asian	10 1-3 >2

Schatzberg and Nemeroff 2004
Mrazek 2006

CULTURAL ASPECTS OF THE PHARMACOLOGICAL MANAGEMENT OF DEMENTIA

Genetic Factors
- Drug Metabolizing Enzymes
- **Antidepressant Ethnic Differences**
- Antipsychotic Ethnic Differences
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- Cognitive Enhancer Ethnic Differences

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ANTIDEPRESSION ETHNIC DIFFERENCES

Asian subjects have a increased likelihood of having genetic background that results in lower metabolic clearance of medications handled by CYP enzymes

Standard doses may result in higher serum concentrations, higher sensitivity to short and long-term side-effects

ANTIDEPRESSANT ETHNIC DIFFERENCES

Higher plasma concentrations after single dose administration has been reported compared to Caucasians for

- Nortriptyline (Japanese)
- Venlafaxine (Japanese)
- Desipramine (Chinese)

No difference reported when compared to Caucasians for

- Sertraline (Chinese)
- Nortryptiline (Hispanics)

ANTIPSYCHOTIC ETHNIC DIFFERENCES

Genetic Factors

- Drug Metabolizing Enzymes
- Antidepressant Ethnic Differences
- **Antipsychotic Ethnic Differences**
- Benzodiazepine Ethnic Differences
- Cognitive Enhancer Ethnic Differences

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ANTIPSYCHOTIC METABOLIC DIFFERENCES

MED	METABOLISM	INDUCER	INHIBITOR
Haldol	3A4	Carbamazepine, phenytoin	Fluoxetine, sertraline, grapefruit juice
Risperidone	2D6>3A4	Carbamazepine, pheytoin, St. John's wort	Paroxetine, fluoxetine, sertraline, grapefruit juice
Aripiprazole	2D6>3A4		
Olanzapine	1A2	Smoking, lamotrigne	Fluoxetine
Quetiapine	3A4>2D6	Carbamazepine, phenytoin	Fluoxetine, sertraline, grapefruit juice

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ANTIPSYCHOTIC ETHNIC DIFFERENCES

Haldol	Higher doses prescribed in AA, Higher rates of side-effects reported in Chinese, Japanese, Koreans in US
Risperidone	Higher % of slow-intermediate metabolizers (2D6) Japanese 40%, Koreans 50%, Chinese 70% African Americans
Aripiprazole	Similar to risperidone but few studies, metabolically neutral ?
Olanzapine	Little data on metabolic differences Asians are prescribed somewhat lower doses than Caucasians, ^risk for type 2 diabetes in Asians
Quetiapine	Higher serum levels more likely due to environmental factors

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BENZODIAZEPINE ETHNIC DIFFERENCES

- Benzodiazepines used for anxiety, agitation, sleep
- Enzyme CYP 3AS handles clearance of benzos
- Significant inter-ethnic differences
- Clearance is lower in Asians compared to Caucasians
- Particularly relevant is prescribing in conjunction with antipsychotics (olanzapine, clozapine)rug Metabolizing Enzymes

CULTURAL ASPECTS OF THE PHARMACOLOGICAL MANAGEMENT OF DEMENTIA

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COGNITIVE ENHANCER METABOLIC DIFFERENCES

MED	METABOLISM	INDUCER	INHIBITOR
Donepazil (Aricept)	3A4 2D6,3A4	Carbamazepine, phenytoin, St. John's wort	Fluoxetine, paroxetine,sertraline, grapefruit juice, liver,renal impairment
Galantamine (Navalin)			
Rivastigmine (Exelon)	Min. hepatic metabolism, renal clearance	Smoking	No reports of drug interactions
Memantine (Namenda)	Min hepatic metabolism, renal clearance	None noted	Severe renal impairment, severe liver impairment?

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Cultural factors affecting attitudes to psychotropic medications

- Biological
  - Nature of psychopathology
    - Dementia vs normal aging
    - Anxiety vs stress
  - Illness-related neurocognitive impairment
  - Current and past experience with medication response and side-effects

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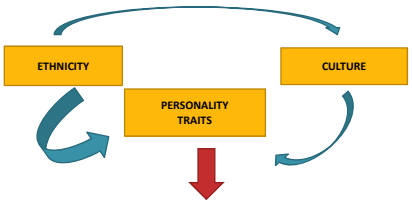

HEALTH BEHAVIORS

Culturally determined personality traits like dependence-independence, orthodoxy-adventuriousness may influence health behaviors such as

Help seeking patterns
Response to medication
Perception of side-effects
Treatment adherence

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CULTURAL FORMULATION INTERVIEW

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CULTURAL FORMULATION INTERVIEW

- Health beliefs
- Alternative treatments
- Support system
- Explanatory model
- Collaborative relationship

CULTURAL FORMULATION INTERVIEW

- Cultural Formulation Interview, (CFI) is meant to be administered during patients' initial assessment
- CFI consists of 14 questions such as:
  - "People often understand their problems in their own way, which may be similar or different from how doctors explain the problem. How would you describe your problem to someone else?"
  - "Is there anything about your background, for example your culture, race, ethnicity, religion or geographical origin that is causing problems for you in your current life situation?"

CULTURAL FORMULATION INTERVIEW

- The CFI allows individuals
  - to define their problems as they see fit
  - to make explicit their own explanatory models
  - to relate this to how others within their social networks (including family members and those that don't share their culture) may see their problems.

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CULTURE AND ATTITUDES TOWARD MEDICATIONS

Cultural factors affecting attitudes to psychotropic medications

- Psychological
  - Illness Explanatory models
  - Lack of medical information
  - Personal meaning of accepting psychiatric treatments (stigma)

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Cultural factors affecting attitudes to psychotropic medications

- Sociocultural
  - Stigma of psychiatric illness and treatments
  - Attitudes of family and support network
  - Nature of relationship with mental health team—"Placebo Effect"
  - Preference for traditional treatments

RELATIONSHIP ISSUES
Patient factors

- Negative attitudes or false beliefs about medications
- Lack of medical knowledge, health literacy, psychoeducation
- Illness explanatory models incongruent with clinician's model
- Lack of social supports
- Cultural/language barriers to care

RELATIONSHIP ISSUES
Clinician factors

- Prescribing practices
  - Haldol, SSRI's, Donepezil, SGA
- Limited time to explore psychosocial needs and conduct referrals
- Limited time for psychosocial and compliance education
- Limited flexibility to change regime in response to side-effects

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  - **Diet ,Habits, Alternative Treatments**

Herbs and CYP3A4

Induction

St. John's Wort

Herb used for mild depression

Induces CYP3A4 enzymes

Speeds metabolism of medication partners

DIET and CYP3A4 Inhibition

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SMOKING

- Decreased blood levels due to induction of liver enzymes
  - Antidepressants (impramine, trazodone)
  - Antipsychotics (haldol, olanzapine)
  - Anxiolytics (xanax, lorazepam, diazepam)

Herbs and CYP 450 enzymes

- Kava Kava
- Herbal treatment for anxiety
- Inhibits numerous CYP 450 enzymes
  - CYP1A2
  - CYP2D6
  - CYP3A4

Cultural Aspects of the pharmacologicaL management of dementia

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CULTURAL ASPECTS OF THE PHARMACOLOGICAL MANAGEMENT OF DEMENTIA

Ng C, Lin K, Singh et al. Etho-psychopharmacology. Advances in Current Practice. Cambridge University Press 2008

Ethnomed. Integrating Culture into Clinical Practice http://ethnomed.org/

Cultural/Ethnic Diversity in Alzheimer's
http://www.alz.org/alzwa/in_my_community_13902.asp

ETHNICITY, RACE AND Non-genetic Factors

- RACE
  - Largely perceived by appearances and attributed to genetic and biological traits
  - Racial differences maintained because of cultural significance

ETHNICITY, RACE AND CULTURE

- ETHNICITY
  - Self/society group construct based on geography, language, religion
  - Race is a component of ethnicity
  - Traditions, values, shared history and generational transmission
  - Ethnic identity is not static and re-shaped by settlements, employment, migration effects

The physician-patient relationship and dynamics of dementia diagnosis live in this dynamic environment

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CULTURE

- Shared system of concepts or mental representations established by convention and maintained by traditional transmission

Q & A

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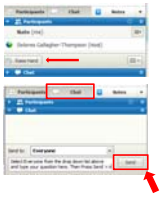

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Final Question
Thank You for Participating!

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