Issues and challenges for psychiatric nurses as they integrate genetic core competencies into their clinical practices

Marilyn A. Davies, RN, PhD

School of Nursing
Objectives

• Describe NCHPEG and ISONG Core Competencies
• Apply Core Competencies to Psychiatric Nursing Practice Situations
• Understand Psychiatric Nursing’s Role in a Genomic Area
National Coalition of Health Professional Education in Genetics NCHPEG Competencies (2001)

• "The future is genetics and it is now!"

• Knowledge (17)
  Skills (17)
  Attitudes (10)

Note: Required Reading
Knowledge (17):

• Basic human genetic technology
• Basic patterns of biological inheritance
• The importance of family history
• The range of genetic approaches to treatment of disease
• The components of the genetic counseling process
Skills (17)

• Gather genetic family history information
• Refer to appropriate genetics experts
• Obtain credible, current information
• Prepare clients and families on what to expect from genetic-counseling services
• Educate clients about availability of genetic testing
Attitudes (10)

• Recognize philosophical, theological, cultural, and ethical perspectives influencing use of genetic information and services
• Appreciate the sensitivity of genetic information and need for privacy and confidentiality
• Willingness to update genetic information at frequent intervals
ISONG core competencies

1. Be Aware of Genetic Information Nondiscriminatory Act (GINA)
2. Safeguard a client’s right to privacy
3. Adopt into practice guidelines for ethical practice
4. Become familiar with legislation with regard to curse/client relationship, confidentiality of medical information
5. Obtain and make a record of informed consent prior to releasing genetic information to any 3rd party
6. Understand that family culture, values, traditions influence the sharing of genetic information
7. Recognize that each individual in the family is autonomous with respect to genetic matters
8. Potential for stigmatization and discrimination as a consequence of genetic info. with ethnicity, race...
9. Educate clients and public about ways tissues and cells can be used as a source of genetic information,
10. Collaborate with other health professionals to assure that clients receive the highest level of genomic health care
Tandem Repeats

• When a pattern of two or more nucleotides is repeated and the repetitions are directly adjacent to each other.
• An example would be:

  ATTCGATTCGATTCG

-STR (short tandem repeats)- repeated DNA sequences that involve a repetitive unit of 1–6 base pairs (bp).
-VNTRs (Variable number tandem repeats)
Example:

Trinucleotide Repeat Disorders

A trinucleotide is a group of 3 chemical bases within a gene. Trinucleotides code for amino acids. Amino acids are the building blocks of proteins.

TRINUCLEOTIDE  C G G

Normal number of repeated trinucleotide segments within a gene = Normal Protein Function.

Mildly expanded number of repeated trinucleotide segments = Normal Protein Function.

Fully expanded number of repeated trinucleotide segments = Abnormal or Absent Protein.
The major histocompatibility complex (MHC) in humans (6p)

• Acts as marker of self and presents antigen to T-helper cells.

• There may be as many as one hundred different alleles at a single locus. The most polymorphic system known.

• If one also considers that an individual possesses five or more HLA loci, it becomes clear why donor-recipient matches for organ transplantations are so rare (the fewer HLA antigens the donor and recipient have in common, the greater the chance of rejection).

Fig. 1. Diagrammatic representation of the human DRD4 gene region. Exon positions are indicated by blocks (yellow, noncoding; orange, coding). The approximate positions of a 120-bp promoter region duplication (blue triangle), an exon 1 12-bp duplication (blue triangle), an exon 3 VNTR (blue triangle), and two intron 3 SNPs are indicated. 2R–11R variants of the VNTR are indicated below exon 3 (blue) along with their worldwide population frequencies determined by PCR analysis (3, 17).
DRD4 related to infant attention and information processing: a developmental link to ADHD?

1-year-old infants with the 7-DRD4 allele showed less sustained attention and novelty preference than do infants without the 7-DRD4 allele.

Impulsivity/ADHD
Anticipation

- Correlates with increasing expansion size.
- Severity of a genetic disease increases with each generation, and/or
- the age at which a disease manifests itself is earlier and earlier with each vertical transmission.
Major cause of neurological disease.

- X-linked spinal and bulbar muscular atrophy (SBMA),
- Two **Fragile X Syndromes** of mental retardation (FRAXA and FRAXE),
- Myotonic dystrophy,
- **Huntington's disease**, 
- Spinocerebellar ataxia type 1 (SCA1), and
- Dentatorubral-pallidoluysian atrophy (DRPLA).

* Some **Early Onset Bipolar Disorder**/Schizophrenia
Fragile X

• Due to a trinucleotide repeat expansion of CGG on the long arm of the X chromosome (Xq27.3) in the FMR1 (fragile X mental retardation) gene
  • Normal individuals have 29-30 repeats, those affected with MR have >200 repeats of the CGG trinucleotide
  • The expansion of copies of the CGG trinucleotide leads to excessive methylation of the cystosines in the promoter region of the FMR1 gene which prevents the normal expression of the gene
Case Studies Presentations and Application
Fragile X

• Most common cause of inherited MR and developmental disabilities

• Approx. 1/3600 -4000 males in the world are born with the full mutation for Fragile X. Note: The vast majority of males with the full mutation will have fragile X syndrome.
  - Approximately 1/ 4000- 6000 females in the world are born with the full mutation for Fragile X.
    Note: Approximately 50% of females with the full mutation will have some features of fragile X syndrome.
  - Approx. 1 /800 men in the world are carriers
  - Approx. 1 /260 women in the world are carriers.

Source: medgen.genetics.utah.edu
Fragile X Syndrome: Anticipation

http://www.google.com/url?sa=t&source=web&cd=4&sqi=2&ved=0CCMQFjAD&url=http%3A%2F%2Fpsych.colorado.edu%2F~carey%2Fcourses%2FPSYC3102%2Fslidesdir%2FHGSS_Chapter5_FragileX.ppt&rct=j&q=ppt%20fragile%20x&ei=FmNhTJruL4T6lwfbz_iTCg&usg=AFQjCNGEn2c7T7JVcPA7OQMqA3s3jkrDwXw

HGSS: Carey, Figure 5.4
Figure C-2: Risk for child of HD individual

Each child has 1 in 2 chance of inheriting the non-HD allele. This is a 50% risk.
Nuclear Family
8/10/10
Discussion: HD

• What are some of the considerations an individual faces when deciding about predictive genetic testing?
• What assistance might you as a nurse offer to individuals considering genetic testing?
• Focus on psychosocial support and advocacy and think about some of the ways you as a nurse could assist an individual who has just found out he/she is positive for the HD mutation.
The Genomic Era

• Technological advances
• Personal Genome Project
• Growing interest among the public
• Advances in pharmacogenetics
Psychiatric Nurse’s Role in the Genomic Era

• Etiology
• Predisposition for disease (risk assessment)
• Treatment
  -genetic testing  -referrals to genetic counselors
• Treatment outcomes
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Enzymes are used to “cut and paste”

• Steps involved:
  Isolate a desired gene using

  **restriction enzymes**: are bacterial proteins that have the ability to cut both strands of the DNA molecule at a specific nucleotide sequence.

  **DNA ligase** “pastes” the DNA fragments together

• The result is **recombinant DNA**
Polymerase chain reaction (PCR)

- method is used to amplify DNA sequences
- The polymerase chain reaction (PCR) can quickly clone a small sample of DNA in a test tube

DNA fingerprinting

- **STEPS**
  - *use non-coding DNA*
    1. Sample DNA cut with restriction enzymes
    2. Fragments separated by size using gel electrophoresis
    3. Fragments with highly variable regions are detected with DNA probe, revealing DNA bands of various sizes
    4. The pattern of bands produced is the DNA fingerprint, which is distinguished statistically from other individuals

Mapping and Sequencing the Human Genome

In February of 2001, the HGP published its working draft of the 3 billion base pairs of DNA in most human cells.

- The Human Genome Project involves:
  - genetic and physical mapping of chromosomes
  - DNA sequencing
  - comparison of human genes with those of other species

Gene therapy

• the insertion of normal genes into human cells to correct genetic disorders.
  - Progress is slow, however
  - There are also ethical questions related to gene therapy

Gene Therapy

- Was felt to hold great promise at the outset of the HGP—has run into some difficulties
- Would be the most direct approach to treating genetic diseases
- Consists of putting a new functional gene into either a somatic or germ line cell
  - The new gene must be delivered to the site of dysfunction
  - The new gene must correctly express itself over time
New NIH Guidelines for Human Stem Cell Research (070909)

- Establish policy and procedures under which the NIH will fund such research, and help ensure that NIH-funded research in this area is ethically responsible, scientifically worthy, and conducted in accordance with applicable law.

- The new Guidelines, as well as a review of the public comments and other information on stem cell research, are available at: [http://stemcells.nih.gov](http://stemcells.nih.gov)
Knowledge:

• Basic patterns of biological inheritance
Mendelian Inheritance Patterns

• Autosomal Recessive
• Autosomal Dominant
• X-linked Recessive
• X-linked Dominant
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The major histocompatibility complex (MHC) in humans (6p)

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* Some **Early Onset Bipolar Disorder**/Schizophrenia
Knowledge (17):

• Basic human genetic technology
• Basic patterns of biological inheritance
• **The importance of family history**
Why is a family health history important?

• Health problems run in families

• Guides screening tests and behavior change
  -The single most effective method of identifying conditions in families that may be inherited is to obtain a family health history (a genetic screen)

• Family history of a condition/disorder may be a “risk factor” in all stages of life (A positive family history increases risk for common diseases by 2-10 times that of the general population)
Knowledge (17):

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• The importance of family history
• The range of genetic approaches to treatment of disease
GWAS

- These have highlighted several novel susceptibility genes (robust levels of significance and have notably been replicated across samples).

- BD: DGKH, CACNA1C, and ANK3
the ‘case of the missing heritability.’

- Psychiatric disorders are polygenic. That means that the contribution of each locus to risk of disease is modest, that cases carry significantly more risk alleles than controls, and that disease risk increases substantially with the total burden of risk alleles carried.

- the identified variants only account for a small fraction of genetic variability.

- GWAS: results are only a **starting point** rather than an end point.
  - many more steps need to be taken to put the pieces together.
The genetic makeup of an organism is called its **genotype**.

What an organism looks like, or what we observe about it, is called its **phenotype**.
Limitations of genetic studies in major mental illness

• Disorders are too broadly defined – potentially use symptom or behavioral phenotypes
• Clinical Heterogeneity (Should focus be on subtypes?)
• There may be more than one etiology/consider comorbidities
• Should major effort be on predisposing/susceptibility genes?
• More consideration of gene-environment effects
Pharmacogenetics

Your DNA Affects Your Response to Drugs
Genes Determine Drug Effects

- Compound
- Absorption Distribution Metabolism Excretion
- Concentration
- Adverse Reactions
- Beneficial Effects
- G-Protein
- Receptor
- Gene
Polymorphisms affecting drug metabolism

- Variations in
  1. drug metabolizing enzymes
  2. prodrug (must be metabolized to active form) metabolizing enzymes
Cytochrome P-450 Polymorphisms

• A hepatic enzyme system involved in the oxidation of many drugs

• Called a ‘superfamily’ of genes and are named in the following way: CYP followed by family number, subfamily letter, and number of the individual form---CYP2C9
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<th>CYP2D6</th>
<th>CYP3A4</th>
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The most relevant Cytochrome P450 enzymes involved in AAD metabolism
Four Phenotypes

• Poor metabolizers (PM)
• Intermediate metabolizers (IM)
• Extensive metabolizers (EM)
• Ultra-rapid metabolizers (UM)
Genes Determine Drug Effects

- Compound
- Absorption Distribution Metabolism Excretion
- Concentration
- Adverse Reactions
- Beneficial Effects
- G-Protein
- Receptor
- Gene
Pharmacogenetics Resources:

- **PharmGED**
  - Pharmacogenetic effect database
- **PharmGKB**
  - Pharmacogenetics & pharmacogenomics knowledge base

www.hsls.pitt.edu/guides/genetics
Knowledge (17):

- Basic human genetic technology
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- The importance of family history
- The range of genetic approaches to treatment of disease

- The components of the genetic counseling process
Genetic Counselors

• Help to translate complicated scientific and medical information into something patients can understand

• Patients are thus informed and empowered to make the decisions that are right for them = nondirectiveness

• Often the topics of discussion have very personal and emotional implications for patients and their families
Skills (17)

• **Gather genetic family history information**

• Refer to appropriate genetics experts

• Obtain credible, current information

• Prepare clients and families on what to expect from genetic-counseling services

• Educate clients about availability of genetic testing
Competencies

• Be able to collect a 3 generation family history (medical and psychiatric)

• Be able to draw and interpret a simple pedigree
Skills (17)

- Gather genetic family history information
- Refer to appropriate genetics experts
- **Obtain credible, current information**
- Prepare clients and families on what to expect from genetic-counseling services
- Educate clients about availability of genetic testing
QUESTION:

?...how to locate the relevant genetic information about a particular disorder...?
Useful (free) Online Resources (1):

• search.HSLS.MolBio
  • Molecular databases & tools search engine, U.Pitt

• NCBI Entrez Gene
  • Searchable database of genes

• Online Mendelian Inheritance in Man (OMIM)
  • Compendium of human genes and genetic phenotypes

• GeneTests
  • Medical genetics information resource

• GARD
  • Molecular Genetic and Rare Disease Information Center

• Genetic Tools
  • Genetics through a primary care lens

www.hsls.pitt.edu/guides/genetics
Useful (free) Online Resources (2):

- **BioMed Central Databases**
  - Catalog of biomedical databases
- **Genetic Association Database**
  - Archive of human genetic association studies
- **Database of Genomic Variants**
  - Curated catalog of structural variants in human genome
- **dbGAP**
  - Database of Genotypes & Phenotypes
- **Gene Gateway**
  - Collection of guides/tutorials on the Human Genome Project
- **Your Genes Your Health**
  - A multimedia guide to genetic disorders

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- **Educate clients about availability of genetic testing**
Genetic Testing: T/F

- There are commercially available genetic tests for the diagnosis of severe mental illnesses
- Most parents would get a genetic test for bipolar disorder if it was available
- A genetic explanation for mental illness is likely to decrease stigma associated with a mental disorder
Attitudes (10)

• Recognize philosophical, theological, cultural, and ethical perspectives influencing use of genetic information and services

• Appreciate the sensitivity of genetic information and need for privacy and confidentiality

• Willingness to update genetic information at frequent intervals
Societal Concerns Arising from the New Genetics

• Fairness in the use of genetic information

• *Who should have access to personal genetic information, and how will it be used?*
  
  ? insurers, employers, courts, schools, adoption agencies, and the military, among others.
Societal Concerns Arising from the New Genetics

- Fairness in the use of genetic information
- Privacy and confidentiality

Who owns and controls genetic information?

2008: Genetic Information Nondiscrimination Act (GINA).

- Forbids insurance companies from discriminating through reduced coverage or pricing and prohibits employers from making adverse employment decisions based on a person’s genetic code.
  - Insurers and employers are not allowed under the law to request or demand a genetic test.
Societal Concerns Arising from the New Genetics

• Fairness in the use of genetic information
• Privacy and confidentiality

• Interpretation of genetic information
  - reliability/validity issues of genetic tests
  - who reviews results and what information is communicated?
Societal Concerns Arising from the New Genetics

• Fairness in the use of genetic information
• Privacy and confidentiality
• Interpretation of genetic information

• Psychological impact and stigmatization

How does personal genetic information affect an individual and society's perceptions of that individual?

Results of studies of persons with BD
Societal Concerns Arising from the New Genetics

• Fairness in the use of genetic information
• Privacy and confidentiality
• Interpretation of genetic information
• Psychological impact and stigmatization

• Educating health care professionals and the public about genome research and its implications

How do we prepare healthcare professionals for the new genetics?
ISONG core competencies

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Case Studies Presentations and Application
Fragile X Syndrome: Case 1

http://www.google.com/url?sa=t&source=web&cd=4&ved=0CCMQFjAD&url=http%3A%2F%2Fpsych.colorado.edu%2F~carey%2FCourses%2FPSYC3102%2Fslidesdir%2FHGSS_Chapter5_FragileX.ppt&rct=j&q=ppt%20fragile%20x&ei=FmNhTJruL4T6lwfbz_iTCg&usg=AFQjCNGEn2c7T7JVcPA7OQMqA3s3JkrDwXw
Fragile X

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Fragile X

• Most common cause of inherited MR and developmental disabilities

• Approx. 1/3600 -4000 males in the world are born with the full mutation for Fragile X.
  Note: The vast majority of males with the full mutation will have fragile X syndrome.
  - Approximately 1/4000-6000 females in the world are born with the full mutation for Fragile X.
  Note: Approximately 50% of females with the full mutation will have some features of fragile X syndrome.
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Case 2: OCD

Nuclear Family
8/10/10

Genetic condition 1
Genetic condition 2
Genetic condition 3
Genetic condition 4
Genetic condition 5
Genetic condition 6
Genetic condition 7
Genetic condition 8
Genetic condition 9
Genetic condition 10
Each child has 1 in 2 chance of inheriting the non-HD allele. This is a 50% risk.
Discussion: HD

• What are some of the considerations an individual faces when deciding about predictive genetic testing?
• What assistance might you as a nurse offer to individuals considering genetic testing?
• Focus on psychosocial support and advocacy and think about some of the ways you as a nurse could assist an individual who has just found out he/she is positive for the HD mutation.
Case 3. Heritability: BD

- Multi-factorial
- Twin/familial studies prove not solely genetic
- 40-70% (some studies up to 85%) risk of developing BPD if your monozygotic twin has the disorder.
- 5-10% risk if your first degree relative has it.
- Multiple Gene Loci
The Genomic Era

• Technological advances
• Personal Genome Project
• Growing interest among the public
• Advances in pharmacogenetics
Future Approaches

Endophenotype

- A trait that is intermediate between genotype and disease, not necessarily beholden to the diagnostic criteria for a single illness, but can help simplify one’s understanding of a complex or heterogeneous disorder
  
  -EX: neurophysiological, biochemical endocrinological, neuropsychological indicator
Examples: Endophenotypes

• MDD-neuroticism (approximately 55% of MDD’s genetic risk many be shared with neuroticism)
• Schizophrenia-processing of sensory inputs
• BD-abnormal regulation of circadian rhythms
The Personal Genome Project

An open-ended research study that aims to improve our understanding of genetic and environmental contributions to human traits

What needs to be done:
- critical mass of interested users
- tools for obtaining and interpreting genome information
- supportive policy, research, and service communities.
Eligibility Requirements

• 21 years of age or older
• Resident/citizen of the United States
• Willing to **publicly** share genetic and trait data
• Any individual employed in the PI's lab or enrollment in a class where the PI provides evaluation of student performance, is ineligible to participate in the PGP.
• You can not enroll in the PGP until all eligibility criteria are met.
• Travel to the medical center in Boston at the participants expense
• Just because you meet the eligibility criteria, it does not mean you will be selected for participation
PGP-10

- The PGP started with 10 participants...the plan is to expand to 100,000 participants
- Currently recruiting for PGP-100
- To come...
  - PGP-1000
  - PGP-10K
Psychiatric Nurse’s Role in the Genomic Era

• Etiology
• Predisposition for disease (risk assessment)
• Treatment
  -genetic testing  -referrals to genetic counselors
• Treatment outcomes (pharmacogenetics)
At a **minimum** be able to:

- appreciate limitations of your genetics expertise,
- understand the social and psychological implications of genetic services,
- know how and when to make a referral to a genetics professional.
- Treat each patient as an individual
- Do not generalize clinical response and patient behaviors based on patient characteristics, particularly race and ethnicity (race and ethnicity are **not** phenotypes)