Sickle Cell Pain: IPRCC Analysis of Current NIH Research

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Sickle Cell Disease Overview

• Rare Autosomal Recessive Hb’pathy (100,000 in US)
• Begins as purely acute-on-chronic, multi-local vaso-occlusive, ischemic and inflammatory pain
• Phenotype transformation to central and/or peripheral neuropathic pain?
• Mechanisms of phenotype transformation?
  – Summative ischemia on neurons?
  – Genetic predisposition (different than 6 beta Hb Val->Glu)
  – threshold effect?,
  – Timing?
• Mechanisms shared in common with other syndromes?
• Approaches to Rx (besides HU and transplant)
  – Opioid?
  – non-opioid chemical?
  – Other, including biobehavioral?
Chronic SCD Pain

- Phenotypic features in common with conditions that exhibit features of central sensitization syndromes?
  - IBS
  - chronic LBP
  - chronic headache
Overview of the portfolio

- Currently 30 grants
- Distributed throughout 6 Institutes
  - NHLBI 23
  - NINR 2
  - NINDS 1
  - NCCAM 1
  - NICHD 1
  - NCMHD 2
Highlights of the Portfolio: Methods

• Total no. SCD grants < any other condition
  – Rare disease
  – relatively recent interest in this field

• Basic and translational research < other conditions
Highlights of the Portfolio: Topics

- Pain outcome assessments and measures 13%
- Health disparities in pain, pain management, and access to care” 11%
- Genetics and genomics of nociception and pain 7%
- Medical management of pain 7%
- Pharmacological mechanisms and treatment 7%
- Development and validation of animal models 9%
- Total 54%
Gaps & Opportunities: Research areas needed or untapped

- Missing studies characterizing SCD pain phenotype(s) or diagnosis/case definitions
  - Ischemic nocioceptive
  - neurological
  - inflammatory
  - Biobehavioral
  - psychosocial

- Missing studies developing analgesics, device, and therapy delivery systems targeted at these mechanisms.
Gap Analysis (cont’d)

• Under-representation:
  – How genetic or other mechanisms alter the SCD pain phenotype
  – Opioid response analysis and studies of new, non-opioid therapeutics

• Areas with 0→2 grants:
  – Pain education, pediatrics, -omics of pain, non—pharmacological mechanisms, and unique populations.

• Lower numbers of grants:
  – pain education, non-pharmacological mechanisms, and biobehavioral and psychosocial mechanisms

• Higher percentage of grants:
  – pain outcome assessments, health disparities, access to care, pain and women’s and minority’s health research
Relevance to other pain conditions and opportunities to collaborate

• Recent collaboration sought between investigators from NHLBI & investigators from NINDS, NICDR, NINDS, NCCAM, and NIDA
  – Example studies: OPPERA (NIDCR) and MAPP (NIDDK)

• Questions
  – How are the pain phenotypes in SCD similar to those of other syndromes?
  – Is the pain phenotype in SCD static or age-dependent and evolving?