

Working Group on the Neurobiology of Pain and the Pharmacogenetics of Opioids in Sickle Cell Disease

Date: April 31—May 1, 2007.

Location: DBDR Conference Room, 6701 Rockledge Dr., Bethesda, MD.

Purpose/Objective: The field of the neurobiology of pain responses has burgeoned in the past ten years. These insights have led to translational studies that have investigated the neurological location of pain perception through imaging modalities, such as functional MRI; variations in patient responses to painful stimuli, and the genetic basis of opiate sensitivity. However, sickle cell disease, a disease in which chronic and acute pain are cardinal symptoms from childhood onwards, has not been a beneficiary of this new knowledge. The purpose of convening this Working Group was to begin to remedy this situation, and to bring together basic researchers and clinical investigators in the fields of pain neurobiology with hematologists who are specialists in the management of pain in sickle cell disease. It is hoped that this colloquy will lead to studies that will specifically investigate the nature of pain syndromes in sickle cell disease, and the inclusion of these subjects in non-disease specific protocols.

Session 1 of the meeting was entitled “Pain in Sickle Cell Disease: Pathophysiology and Clinical Syndromes”. The session began with presentations, by two hematologists with expertise in sickle cell disease and specifically, the management of pain. James Eckman, MD (Emory) talked about the spectrum of acute pain in SCD, while Lennette Benjamin (Einstein) discussed the chronic pain syndromes in this disease. Julia Finkel, MD, an anesthesiologist at Children’s Hospital, Washington, DC, who specializes in the management of pain, spoke of the specific pain mechanisms that occur, and how rational choices of analgesics can be made.

Session 2, “Neuronal Mechanisms of Pain and Their Modulation” began with a talk by Clifford Woolf, MD, PhD, (Harvard) that was a broad overview of current hypotheses on the physiology of pain, together with recent findings from his laboratory concerning the genetics of pain responses. Gerald Gebhardt, PhD, (Pittsburgh) discussed “Mechanisms of Hypergesia”.

Session 3, “Responses to Pain”, began with Robert Coghill, PhD, (Wake Forest) on “Neural Correlates of the Subjective Response”, where he presented his findings on the role of previous experience and emotions in pain responses, as detected by functional MRI (fMRI). Sean Mackey, MD, PhD, (Stanford) next continued with this topic in “Emotional and Cognitive Factors in Pain”. David Borsook, MD, PhD, (Harvard) spoke on “The Utility of fMRI in Pain and Analgesia”. Finally, Jennifer Haythornthwaite, PhD, (Johns Hopkins) discussed cognitive behavioral therapy for chronic pain. This ended the first day’s sessions.

The next day began with Session 4, “Pharmacogenetics of Chronic Pain Susceptibility and Analgesic Response”. Jeffrey Mogil, PhD, (McGill) talked about mouse models of pain, in “Genetics Determinants of Pain”. Jim Wang, PhD, (University of Illinois at Chicago) spoke about “Polymorphisms of Neurotransmitter Receptors and Individual Responses to Pain”. Kathleen Neville, MD (University of Missouri, Kansas City), delivered David Flockhart’s (Indiana) talk in his absence, “Issues in Pharmacogenetics in African-Americans”. Robert Molokie, MD (University of Illinois at Chicago) spoke on “Studies of Pharmacogenetics of Opioids in Sickle Cell Disease.” Dr. Neville then discussed “Developmental Pharmacology in Children: Implications for Sickle Cell Disease Pain and Analgesia.”

This ended the formal presentations. The last hour was devoted to a discussion on future directions in pain research in sickle cell disease. all of the participants were enthusiastic about the great unmet potential to utilize the methodologies of neurobiologists and clinicians who specialized in pain research to sickle cell disease. they strongly supported the issuance of an RFA on this subject.

Outcome: I presented a proposal for an Initiative to the NHLBI Idea Forum on December 6, 2007. This is the first step in the process for approval of candidate RFA's. I had support for this initiative from representatives of two other ICs, NIDA and NINDS. I am currently reworking my initiative, in response to suggestions by the other participants in the Idea Forum. A decision concerning which Initiatives will be further developed into RFA will be made in the spring of 2008.

Publication Plans: None, as of now.

Participating Divisions: NHLBI/DBDR, NIDA, NINDS, Office of Rare Diseases.