

## Meeting Summary

The Fifth Scientific Meeting of The TMJ Association: Can Studies of Co-Morbidities with TMJDs Reveal Common Mechanisms of Disease?

June 1-3, 2008

FASEB Conference Center, Bethesda, MD

The meeting was organized and supported by The TMJ Association with co-sponsorship by eight Institutes, Centers and Offices of the National Institutes of Health. Earlier studies indicated that many patients with temporomandibular joint disorders suffer a range of comorbid conditions including chronic headache, generalized pain conditions, irritable bowel syndrome, endometriosis, interstitial cystitis, vulvodynia, fibromyalgia, chronic fatigue syndrome, and rheumatoid arthritis. The meeting sought to determine if there are common genetic factors and mechanistic pathways that link these comorbidities, accounting for their co-occurrence in patients.

The meeting began with a patient round-table discussion. Representatives from several advocacy groups presented their views on the most pressing research questions facing their respective disorders and how these groups might work together in achieving a better understanding of the commonalities among their disorders. This was followed over the next two days by twenty-three scientific presentations in seven different sessions from both junior and senior scientists, usually paired together, to address the basic science and the clinical aspects of each of these chronic pain conditions. There was an extensive discussion period following each session. In addition, posters were presented by young investigators during the meeting in two sessions. On the final day, three breakout groups met to discuss commonalities in the basic science, clinical features, and potential diagnostic approaches and biomarkers of these disorders. The NIDCR Director provided introductory and closing remarks for this meeting. The Director of NCRR and a program representative of NIBIB also provided opening comments.

### Research Recommendations

Following presentations and discussions by experts in the selected conditions as well as patient testimony, attendees met in planning sessions to develop research recommendations to advance understanding of the etiology and pathogenesis of these disorders and guide the development of diagnostics and therapy for all of these conditions.

The attendees concluded that chronic debilitating pain was the feature most shared among the comorbid conditions discussed. Chronic pain is a condition that transcends the boundaries of biomedical research and clinical specialties as well as the mandates of the categorical Institutes and Centers of the NIH. As such, a focus on chronic pain research will provide a major opportunity to fill a

gap in biomedical research, one which no single component of NIH should or could tackle alone. The following recommendations were presented at the close of the meeting and further refined by the Program Committee.

The primary recommendation that emerged from the meeting was to launch a genome-wide association study (GWAS) to identify genes associated with chronic pain across a wide spectrum of persistent pain conditions. It was recommended that this research would be conducted in two phases.

Phase I. This would entail conducting a large-scale case-control genome-wide SNP analysis on patient populations suffering from common persistent pain conditions. The goal of the Phase I GWAS screen would be to identify putative risk factors (i.e., intermediate and endophenotypes) and to identify genetic variants (e.g., haplotypes and genes) related to chronic pain and the intermediate and endophenotypes that are measured in common across the different patient populations.

Phase II. Given genes that have been identified as common to pain in TMJDs and comorbid pain conditions, Phase II recommendations call for studies to determine if there are sets of genetic polymorphisms and functional pathways related to each of the disease-specific syndromes. Phase II studies would be hypothesis-driven with prospective and longitudinally designed studies that would include research related to mechanisms of transitioning from acute to chronic pain, identification of genetic markers and risk factors, strategies for building interdisciplinary and multidisciplinary research teams, and novel tools required for such research.

An important question to be explored would be how acute pain conditions evolve into sustained chronic pain conditions, even in the absence of the initial stimulus.

Another important component of Phase II would test specific hypotheses related to genetic and phenotypic commonalities among the comorbid conditions.

A final key recommendation that emerged from the meeting was to develop innovative approaches required for the successful creation and operation of the interdisciplinary and multi-disciplinary teams required for Phase I and Phase II studies. It was proposed that strategies be put in place to reward data sharing and cross-fertilization of ideas to counter the prevailing scientific culture which currently rewards individual scientists and laboratories. Mechanisms to create a suitable environment for multi- and interdisciplinary research should be explored.

### Tools Development

Presently there are gaps in phenotyping tools, particularly with respect to capturing aspects of comorbidity and environmental risk factors. It will be important to apply and develop standardized measures of signs and symptoms

that define these disorders and enable the clearest possible characterization of the natural history of these conditions. Improved versions of existing tools with better resolving power are needed for phenotyping, along with the application of novel technologies such as those emerging in the fields of genomics, proteomics, and non-invasive imaging and spectroscopy.