Clinical Nerve Function Studies and Imaging

I. General considerations for the use of nerve function and imaging studies
   A. Be aware that no objective measure of ongoing pain is available. The gold standard for assessing pain is the subjective report of the individual. This can be supplemented by observation of facial expression, posture, and other behavioral indices.
   B. Laboratory tests, however, can provide objective evidence for positive and negative sensory phenomena and differential involvement of nociceptive and non-nociceptive afferents (Cruccu et al. 2004).

II. Electrical nerve stimulation (Kimura et al. 1994; Nuwer et al. 1994; Treede 2003; Cruccu et al. 2004)
   A. Be aware that the large myelinated afferents of the tactile system have the lowest threshold to electrical stimuli and hence are predominantly assessed with standard methods of clinical neurophysiology.
   B. Know that the measurement of sensory nerve conduction velocity can demonstrate the loss of A-beta afferent fibers, but is insensitive to selective loss of A-delta and C fibers.
   C. Know that somatosensory evoked potential studies can provide detailed information on the location of a lesion along the somatosensory pathways of the lemniscal system, but are insensitive to selective lesions of the nociceptive system.
   D. Know that some trigeminal (Blink reflex, masseter inhibitory reflex) and spinal reflexes (withdrawal reflex) have both nociceptive and non-nociceptive components that can be exploited in the differential assessment of some lesions.

   A. Be aware that large myelinated afferents of the tactile system are insensitive to heat stimuli and that rapidly rising heat stimuli are an appropriate tool to assess the function of nociceptive pathways.
   B. Know that laser evoked potentials have been validated as sensitive tools to assess deficits of small-fiber function, the spinothalamic tract, and other parts of the nociceptive system in individual patients.
   C. Be aware that laser evoked potentials are sensitive to changes in attentional state.

IV. Quantitative sensory testing (Gracely et al. 1988; Arezzo et al. 1993; Yarnitsky et al. 1995; Ziegler et al. 1999; Greenspan 2001; LeBars et al. 2001; Cruccu et al. 2004)
   A. Know that quantitative sensory testing can be used to test large and small nerve fiber function.
   B. Know that vibration and brushing detection is mediated by A-beta fibers.
   C. Know that cool detection thresholds depend primarily on A-delta-fiber function.
   D. Know that warm detection thresholds depend primarily on C-fiber function.
   E. Know that pain evoked by pinpricks depends primarily on A-delta-fiber function.
   F. Know that heat pain thresholds depend on A-delta and C-fiber function, but that slowly increasing temperature changes preferentially recruit C fibers and rapidly increasing temperatures recruit A-delta fibers.
G. Know that cold pain threshold primarily depends on C-fiber function.

V. Skin biopsies (McArthur et al. 1998; Nolano et al. 1999; Cruccu et al. 2004)
   A. Be aware that innervation density by sensory nerves, including C fibers, can be assessed in skin punch biopsies.
   B. Know that skin biopsies are more sensitive and less invasive than nerve biopsies.

VI. Magnetic resonance imaging (May et al. 1999; Davis 2000; Tracey 2001; Grachev and Apkarian 2002)
   A. Be aware that functional magnetic resonance imaging (fMRI) can provide indirect information on brain activity through hemodynamic measures.
   B. Know that fMRI provides better temporal resolution than positron emission tomography (PET).
   C. Know that structural MRI can be used to examine morphometric changes in the brain related to chronic pain conditions.
   D. Know that magnetic resonance spectroscopy can be used to examine brain chemistry.

VII. Positron emission tomography (Jones et al. 1991; Talbot et al. 1991; Tölle et al. 1999; Casey et al. 2000; Zubieta et al. 2001)
   A. Be aware that PET can provide indirect information on brain activity (hemodynamic or metabolic imaging) and neuropharmacology (receptor imaging).
   B. Know that radioligands can be used to image availability of neurotransmitter binding sites, and thus potentially assess degeneration, receptor internalization, and endogenous ligand occupation in the presence and absence of different types of pain.
   C. Be aware that PET has poor temporal resolution.

VIII. Electro- and magnetoencephalography (Anogianakis et al. 1992; Schnitzler and Ploner 2000; Garcia-Larrea et al. 2003; Schlereth et al. 2003)
   A. Know that electroencephalography (EEG) and magnetoencephalography (MEG) reflect the synaptic activity in the brain.
   B. Be aware that EEG- and MEG-source analysis has a limited spatial precision of about 10 mm, but unsurpassed temporal resolution.

   A. Know that the basic pattern of brain activation with acute painful stimuli includes thalamus, primary somatosensory cortex, operculo-insular cortex, cingulate cortex, prefrontal cortex, and cerebellum.
   B. Be aware that certain aspects of the brain activation patterns may differ among pain states (e.g., cutaneous vs. visceral; acute vs. chronic) and may be modulated under hyperalgesia or allodynia.
   C. Know that brain imaging can be used to examine the basis of pain modulation by psychological factors such as attention, emotion, and expectancy.
   D. Know that brain imaging can be used to examine the forebrain mechanisms of analgesia (e.g., opioid analgesia, placebo analgesia).
   E. Be aware that PET and fMRI analyses involve statistical tests and therefore can prove the presence but not the absence of activation in a given region.
REFERENCES


