Transition to chronic pain: opportunities for novel therapeutics


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Supplementary Figure 1: The transition to chronic pain. Individuals have a pre-existing set of risk, or potentially, resilience factors, that may predispose them to transitioning to chronic pain following any number of events shown in the second rectangle. During this process, several mechanisms can be engaged. These mechanisms may occur together, or in isolation, and promote pain persistence. Chronic pain is also frequently associated with significant comorbidities, which have a profound impact on quality of life, but their development is not well defined mechanistically.
Supplementary Figure 2: Key questions in the transition to chronic pain. An acute pain stimulus can trigger neuronal, immune or neuro-immune mechanisms that lead to a chronic pain state. One key question is whether these mechanisms can be targeted for the prevention or reversal of the chronic pain state. It is also possible that there is only a limited temporal window during which these mechanisms can be targeted to reverse a chronic pain state. Pain resolution mechanisms, which may be separate from pain chronicity mechanisms shown in the thick downward arrows, might also be engaged to terminate chronic pain states. As the duration of chronic pain increases, the presence of comorbidities increases, often leading to disability. Another key question is whether it is possible to reverse long-standing chronic pain states or their varied neurological consequences. It may be feasible to reach a new, acceptable homeostatic set point with a meaningful level of pain relief, but without a full reversal of the underlying neuronal or immune plasticity. Pain resolution mechanisms able to reverse even long-standing chronic pain would have the largest impact because they would restore function to the greatest extent possible.