International Collaboration On Neuroinflammation in Traumatic Brain Injury, (ICON-TBI)

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Traumatic brain injury (TBI) is commonly thought of as an acute self-limited problem. However, in many patients, it can result in chronic disability. In a sizeable minority, such disability can be progressive. Indeed, we now know that either a single severe TBI, or repeated mild TBI, can substantially increase the risk of late dementia. It is believed that a substantial part of these late effects of TBI may be driven by brain inflammation. Indeed, we have known for a long time that patients who suffer a severe TBI have significant acute inflammation in the brain. However, there is increasing evidence that this process may also be important in milder forms of TBI, and that it can become a chronic process. Intriguingly, there are suggestions from animal models of TBI that some of this chronic inflammation may be because the body develops an immune response against the brain, but it is not clear whether this process is beneficial or harmful to patients. We plan to investigate this issue by studying 175 patients with a range of TBI severity. We will look at the levels of inflammatory cells and molecules in both blood and brain fluids, and compare this with a technique called positron emission tomography (PET), which uses small doses of radioactive tracers to image brain inflammation, and with serial magnetic resonance imaging to map the impact of such inflammation. These clinical studies will be underpinned by a portfolio of animal studies which will obtain more detailed information on the types of brain inflammation that occur after TBI, understand what drives it to produce harm or benefit, and investigate the effect of novel drugs in improving this process. We believe that our research may allow us to identify patients who develop chronic inflammation, differentiate those who experience harm from those who benefit from this process, and provide drugs that might be used to control this process in specific subgroups of patients. This holds the promise that we may be able to identify drugs that act more precisely, and match them to the needs of specific patients. This would represent a substantial advance on the present context, where we use drugs that have very wide actions on inflammation across an entire population of patients, and run the risk that many of these patients may not experience any benefit from the drug, but still be at risk of harm from its side effects.