

Where do we go in occupational neuroepidemiology?

Early knowledge about the neurotoxic effects of occupational exposures appeared through clinical observations. The observed effects were more or less acute and concerned exposure to metals such as lead and mercury or solvents like carbon disulfide and trichloroethylene. With time, however, also more chronic and clinically less obvious effects of neurotoxic agents have been assessed through modern examination methods and systematic studies of larger groups. Still, the interpretation of the findings has been controversial and debated, such as the chronic effects of solvent exposure (1).

The difficulties met in interpreting chronic neurotoxic effects depend on both the diversity and vagueness of symptoms and signs and the associated problem of defining a proper disease entity for conclusive epidemiologic studies. For example, in solvent exposure, the chronic effects might include memory and concentration problems, tiredness, lack of initiative, affect lability, irritability, and sometimes dizziness, headache, alcohol intolerance, and reduced libido. Neurophysiological methods have also revealed various functional disturbances, again difficult to condense into any single disease entity.

Similarly, a variety of neurobehavioral effects also seems to occur due to other occupational exposures, such as moderate lead exposure or welding with some exposure to aluminum, lead, and manganese or exposure to pesticides. Again there are also neurophysiological or neurological signs, among others, polyneuropathy, tremor, and disturbance of equilibrium, in individuals exposed to organochlorine, organophosphorus and other insecticides.

In view of the epidemiologic problems involved in defining a disease entity out of the many types of neurobehavioral effects referred to, it has also become natural to consider some clinically, more or less well-defined neuropsychiatric disorders in relation to occupational exposures.

Since the 1970s, several studies have especially focused on solvent exposure and the psychoorganic syndrome, when of disabling severity. More recently also Alzheimer's dementia, multiple sclerosis, Parkinson's disease, amyotrophic lateral sclerosis, and related conditions have attracted interest in occupational epidemiology.

Regarding solvent exposure and the psychoorganic syndrome (or toxic chronic encephalopathy in clinical occupational medicine, when exposure is taken into diagnostic account), the problem of defining a proper disease entity was apparent and it first led to considering *en bloc* the diagnoses of encephalopathy, dementia, and cerebral atrophy, but also neurosis, neurasthenia, and nervositas were included as not necessarily distinct from each other in medical practice (2). Recently, more specific disease entities, such as organic dementia and cerebral atrophy, have also been associated with solvent exposure (3). The findings have not been totally consistent, however, as no excess of "presenile dementia" appeared in a large-scale case-referent study in the United States with as many as 3565 cases of various neuropsychiatric disorders and 83 245 hospital referents (4). However, in comparison with bricklayers, there was about a 45% excess of disabling neuropsychiatric disorders among white male painters, except spray painters.

Occupational exposures also seem to play a role for disorders more specific than the psychoorganic syndrome. Hence, in 1982, an association between multiple sclerosis and solvent exposure from glues was first indicated in the Italian shoe industry (5). This relationship has been considerably strengthened by further studies in Scandinavia (6—8) and elsewhere, so that 13 studies with some information on solvent exposure could be considered in a review (9). Ten of these studies provided enough data for inclusion in a meta-analysis, showing about a twofold risk for multiple sclerosis among individuals with

solvent exposure. Some studies also associate multiple sclerosis with radiological work, welding, and work with phenoxy herbicides (6—7).

Parkinson's disease seems to be more common in rural areas (10), especially at younger ages (11). More interestingly, a study from Calgary, Canada, showed a threefold risk for herbicide exposure (12). All the case persons who recalled specific exposures reported exposure to phenoxy herbicides or thiocarbamates. One of them recalled exposure to paraquat, which is chemically similar to MPTP (N-methyl-4-phenyl-1,2,3,6-tetrahydropyridine), an inducer of a Parkinson-like syndrome. Paraquat workers have not yet been found to suffer from such a syndrome, however (13). Case-referent studies from Canada, China, Spain, and Sweden have indicated a relation with exposure to unspecified industrial chemicals, pesticides, and metals, especially manganese, iron and aluminum (14).

In a study from the United States, an increased risk of motor neuron disease (encompassing amyotrophic lateral sclerosis, progressive bulbar palsy and progressive muscular atrophy) appeared in connection with welding and soldering (15). Welding also appeared as a risk factor, as did electricity work, and also work with impregnating agents in a Swedish study (16). Heritability for neurodegenerative and thyroid disease, combined with solvent exposure and male gender, showed a risk as high as 15.6. Other studies also indicate that exposure to lead and solvents could be of importance (17—20).

For Alzheimer's disease, no clear indication of any occupational risk appeared in a meta-analysis of 11 case-referent studies (21), but more recently an increased risk was connected with blue-collar work (22). Another new study, which included also the oldest ages, indicated that solvent exposure could be a rather strong risk factor (33). The recent suggestion that Alzheimer's disease might be related to exposure to electromagnetic fields was perhaps even more surprising (44). Both these studies are likely to stimulate interest in several new investigations along the indicated lines.

Hence, in view of the current perspectives in occupational neuroepidemiology, as briefly outlined, there seems to be a reason for conducting additional work-related studies of different, hitherto more or less neglected, neurological and neuropsychiatric disorders. It is not unlikely that there are some contributing effects from various occupational exposures, in the same manner as we have seen for many cancer types. In addition, as in etiologic cancer research, new clues suggesting ultimate causes or triggering mechanisms behind some of the serious neurological disorders may be obtained from occupational epidemiology.

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