MRI classification system (MRICS) for children with cerebral palsy: development, reliability, and recommendations

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ABBBEVIATIONS

MRICS	MRI classification system
PVL	Periventricular leukomalacia
SCPE	Surveillance of Cerebral Palsy in Europe

AIM To develop and evaluate a classification system for magnetic resonance imaging (MRI) findings of children with cerebral palsy (CP) that can be used in CP registers.
METHOD The classification system was based on pathogenic patterns occurring in different periods of brain development. The MRI classification system (MRICS) consists of five main groups: maldevelopments, predominant white matter injury, predominant grey matter injury, miscellaneous, and normal findings. A detailed manual for the descriptions of these patterns was developed, including test cases (www.scpenetwork.eu/en/my-scpe/rtm/neuroimaging/cp-neuroimaging/). A literature review was performed and MRICS was compared with other classification systems. An exercise was carried out to check applicability and interrater reliability. Professionals working with children with CP or in CP registers were invited to participate in the exercise and chose to classify either 18 MRIs or MRI reports of children with CP.
RESULTS Classification systems in the literature were compatible with MRICS and harmonization possible. Interrater reliability was found to be good overall (k=0.69; 0.54–0.82) among the 41 participants and very good (k=0.81; 0.74–0.92) using the classification based on imaging reports.
INTERPRETATION Surveillance of Cerebral Palsy in Europe (SCPE) proposes the MRICS as a reliable tool. Together with its manual it is simple to apply for CP registers.

Surveillance of Cerebral Palsy in Europe (SCPE) has, through agreement in definitions and classifications of cerebral palsy (CP), developed a common language in the domain of CP.[1,2] This has been a prerequisite for comparative studies,[3,4] and for studies which necessitate a large population basis.[4,5] This common language has generated a lot of interest even beyond Europe: the definitions and classifications are widely used, and SCPE papers extensively cited.

CP is a clinical diagnosis, based upon neurological symptoms and a motor disorder causing an activity limitation.[6] SCPE does not consider neuroimaging a prerequisite for the diagnosis of CP.[2] Up to now, normal magnetic resonance imaging (MRI) does not exclude the diagnosis of CP. Moreover, neuroimaging, especially MRI, is not available nor used in all countries to the same extent. In addition, the use of MRI, as well as knowledge of its role in the understanding of CP pathogenesis, has dramatically increased during the last 15 years, which would make comparison between countries and time periods difficult. Most importantly, there is no commonly agreed neuroimaging classification for CP at this time.

Although neuroimaging is not part of the CP definition, neuroimaging findings are abnormal in more than 80% of children with CP,[7–9] disclosing the pathogenic pattern responsible for the CP. Neuroimaging may also help to understand the structure–function relationship.[10,11]

National guidelines recommend MRI as the first diagnostic step after history taking, neurological examination, and examination of additional impairments.[12] Therefore, a need was expressed for the development of a classification system for neuroimaging findings in CP, which could be introduced into the standard CP evaluation form to be prospectively used in registers. For this purpose, a simple system is needed, which can be applied easily not only by

clinicians, but also by epidemiologists or other professionals who work in CP registers. In CP registers, in most cases only a written description of the imaging findings is available and not the image itself. The classification therefore has to be applicable also for the written descriptions.

With the aim to develop such a classification, SCPE had as a first step identified MRI patterns known to be associated with a high risk of CP. CP is defined as a disorder due to a non-progressive interference or lesion or abnormality of the developing or immature brain.[1] Thus, it seemed important to identify patterns according to their time of occurrence during brain development, on the basis that the human brain undergoes complex organizational changes during intra- and extrauterine development; the patterns of abnormalities or lesions found will depend on the stage of brain development at the time of insult.[13] Thus, the brain pathology of CP is dependent on the time of occurrence of noxious events interfering with brain development or actually damaging it. MRI has good potential to visualize this pathology. During the first and second trimesters, predominantly cortical neurogenesis takes place, characterized by proliferation, migration, and organisation of neuronal precursor cells, then neuronal cells. Disturbances in this process result in maldevelopments such as lissencephaly, pachygyria, or polymicrogyria. When affecting the motor cortex, CP may be the result. Some of these disorders may be of genetic origin, especially when symmetrical in distribution.[14]

During the third trimester, when the 'gross architecture' of the brain (neural cyto- and histogenesis) is largely established, growth and differentiation events are predominant and persist into postnatal life (axon, dendrite and synapse formation, myelination). Disturbances of brain development during this period mainly result in clastic lesions. The causes are multiple and key factors are inflammation with excessive cytokine production, oxidative stress, and excess release of glutamate triggering the excitotoxic cascade, factors that are induced by hypoxic–ischaemic and/or infectious mechanisms, whereby a potentiation of single effects can be assumed.[15] Early in the third trimester white matter is especially affected. The major neuropathology potentially damaging the motor tracts and thus leading to CP includes periventricular leukomalacia (PVL) or complications of intraventricular haemorrhage: predominant white matter injury. This pathology has been called 'encephalopathy of prematurity' and is accompanied by 'neuronal/axonal disease'. This may also involve the thalamus, basal ganglia, cortex, brainstem, and cerebellum,[16] although the pathology that is related to CP and identifiable by visual inspection is mainly that of white matter injury.

Lesional patterns that can occur in central motor domains and thus cause CP in the late third trimester concern the cortical grey matter, basal ganglia, and thalamus:[17] predominant cortical or deep grey matter injury. Infarcts of the middle cerebral artery are reported mainly in children born at or near term with unilateral spastic CP.[18] They may also occur in the very-preterm child, then involving more the lenticulostriate arteries.[19]

Thus pathological patterns, characterizing disturbance of early brain development and likely to cause CP, can be summarized as maldevelopments, predominant white matter injury, and predominant grey matter injury; we called these patterns 'pathogenic patterns' because they characterize specific timing periods of disturbance/insult to the developing brain.

In a second step, we had systematically searched in the literature for these pathogenic patterns in children with CP.[7] In this earlier review, MRI was reported to be abnormal in 86% of the CP cases and indicated the pathogenesis in 83%. Periventricular white matter injury was the most frequent finding (56%), followed by deep grey matter injury (18%), and brain maldevelopment (9%). Thus, this earlier review indicated that the classification based on pathogenic patterns covers the main brain pathology in children with CP and seems a useful approach also for CP registers.

The aim of this study was to develop an MRI classification for CP research, registers, and clinicians, compare it with other classification systems used in the literature, and test its reliability.

What this paper adds

- MRI Classification System (MRICS) is a mainly qualitative classification system for children with cerebral palsy (CP).
- MRICS describes pathogenic neuroimaging patterns related to timing of brain compromise.
- The classification system proved to be reliable and easy to use for CP registers.
- MRICS was compared with other classification systems and harmonization was feasible.

METHOD

The development of a classification system was based on the concept of the underlying pathogenic MRI patterns in children with CP. Typical illustrations of these patterns including subgroups and descriptions in the context of clinical cases were searched for and agreed on by the authors. A manual was developed in the process and tested with respect to comprehensibility and applicability during several SCPE workshops. Type of CP and gross motor function according to Gross Motor Function Classification System (GMFCS)[20] were described together with MRI findings.

A literature review was performed, searching for other classification systems of MRI findings in CP, with the question of compatibility with the MRI classification system (MRICS), and whether harmonization between classifications was possible. This review covered the time period January 2007 to March 2013. The following keywords were used for the search: cerebral palsy, neuroimaging, MRI, classification.

A workshop with SCPE participants aimed at harmonizing the findings of the different classifications with the MRICS.