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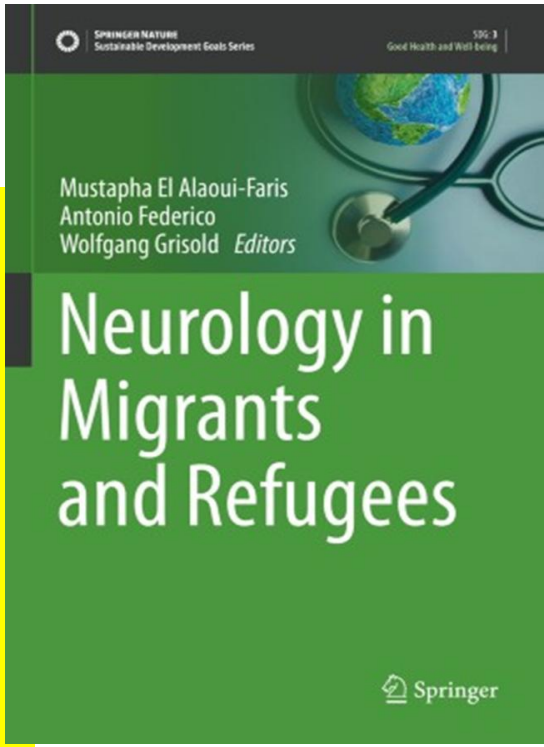
Contribution of migration to Neurosciences



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- In the last decades, migration for different reasons in many world areas (with more than 2 hundred million immigrants or refugees, with numbers doubled in the last 50 years) opened many political, social, economic, sanitary and organization problems.
- This new situation also encouraged some research developments mainly concentrated on the knowledge of the migrant diseases variety (many times little known in the hosting countries), on the migrant access to the host country health system, but also on the possibility that a different genetic background may influence the pathophysiology of several disorders, and on the role of stress, deprivations and change of natural environment on human behavior and brain functions during development and aging

Some aspects of the link between migration and neurosciences

- Migration and risk of several common neurological diseases as cerebrovascular (stroke), degenerative (dementia), inflammatory (multiple sclerosis) and other disorders
- Specific brain diseases in immigrants and refugees
- Migration and access to host country health services
- Contribution to the knowledge of gene mutations involved in dementia, Parkinson, ataxia and other genetic disorders in large families migrating in different countries
- Improvement of diagnosis of rare neurodegenerative and neurometabolic diseases in refugees from countries where consanguinity is frequent with consequent possibility of treatment in some
- Child Migration and neuropsychology
- Migration, brain development and aging
- Correlations between neuropsychological and brain changes in functional MR experiments in refugees
- Possible effect of bilinguism as protection in cognitive disturbances

The relationship of refugee status and migration with the neurological health system has been also utilized as a model to control the efficiency of the host country's health system.

We summarize here some examples of the most interesting data in neuroscience and neurology research on the different aspects of migrant and refugee populations and their relationship with the most common neurological disorders.

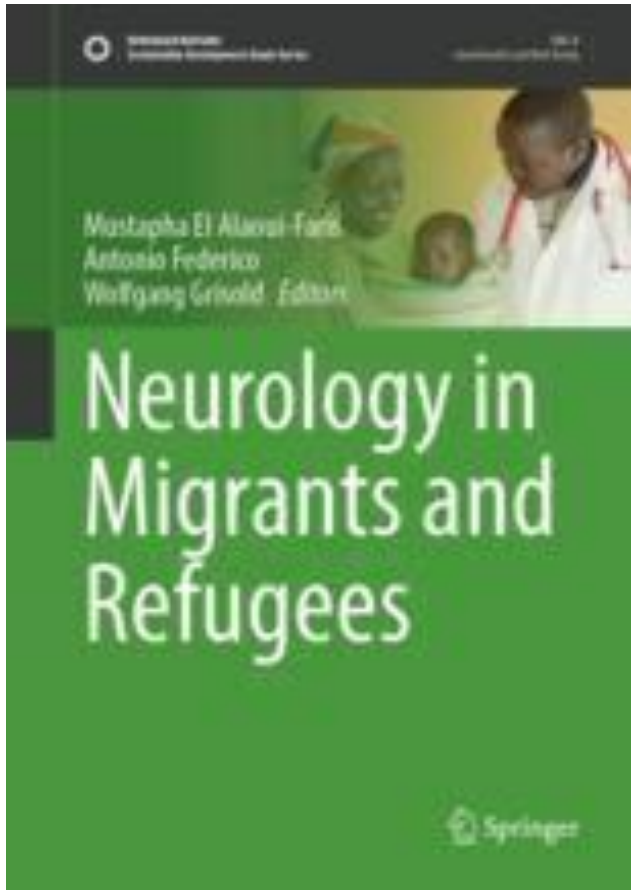
PUBMED data on migration and refugees and neurology and neurosciences

Keywords	Years of publication	Number of articles
Immigrants and neurology	1968–2020	336
Immigrants and neurological diseases	1948–2020	1582
Immigrants and neurosciences	1955–2020	305
Refugees and neurology	1988–2020	61
Refugees and neurological diseases	1948–2020	336
Refugees and neurosciences	1991–2020	161

For all a pick of articles in the last 10 years is present.

Neurologists in Training and Education Programs on Immigrant Health

In 2016, a group of young neurologists in training from the European Academy of Neurology (European Association of Young Neurologists and Trainers), collected results by a questionnaire regarding **Global Health Education in the different training systems in Europe**, describing a **limited education in the curricula regarding women's or children's health and neurological disorders of immigrants and refugees and generally on the global impact of neurological disorders** (Sauerbier et al. 2016). The authors, consequently, invited different institutional organizations and scientific societies to stimulate the authorities to cover this gap.



Neurology in Migrants and Refugees

Editors:

El Alaoui Faris, Mustapha, Federico, Antonio, Grisold, Wolfgang (Eds.)

Activity performed on behalf the WFN Specialist Group on Migration and Neurology

Hosting Health System and Migration

- **A general overview of the health needs of migrating people and refugees has been described by many official institutional documents and reports** (Bradby et al. 2015; Migration and Health in the European Union 2016; Pavli and Maltezou 2017; Khullar and Chokshi 2019).
- Although neurological diseases represent a low prevalence aspect of the global health needs for migrants and refugees, interesting data reports the use of neurological hospital services by migrants and the general organization of the hospitals.
- **Rinaldi et al. (2012) showed that the average length of hospitalization in a north Italian Hospital was significantly longer in immigrant population and that the use of neurological services by migrants is less diffuse than their demographic share**. Poorer economic and social conditions, as well as a worse labor market experienced by immigrants may expose them to risk factors for injuries and infective diseases. Reducing the language and bureaucratic barriers, as well as enhancing cross-cultural skills of physicians, might be crucial in decreasing the length and the cost of hospitalization (Rinaldi et al. 2016).

Hosting Health System and Migration

- More recently Giuntella et al. (2018) evaluated the relationship between the immigration's reason and the immigrations' health in the UK: their results indicate that, in general, immigrants are less likely than natives to report suffering from a long-lasting (1 year or more) health problem. This pattern generally remains the same when we consider the specificity of the long-lasting health problems. **However, marked differences related to the immigration reasons greatly influence these results. Those who migrated for employment, family and study reasons report better health outcomes than natives, while worse health outcomes than natives have been reported by those who migrated to seek asylum**. There is convergence to natives' health outcomes over time for those who migrated for non-asylum reasons, but not for those who migrated to seek asylum. The findings show that the prevalence of health problems differs not only between natives and immigrants but also across groups of immigrants who moved to the UK for different reasons.
- **Moullan and Jusot (2014) investigated the different health immigrant effect in the European countries showing that after controlling for socio-economic status, immigrants have a poorer health status than natives in France, Belgium and Spain, whereas a better health status than natives is present in Italy, among both women and men**. A South-North gradient in immigrants' health status seems to exist, with better condition in Italy and in Spain than in France and Belgium. Conversely, health status of natives is poorer in Italy and in Belgium than in France and in Spain. They conclude that differences in health gap reflect differences in health status of both natives and immigrants between host countries. This suggests differences in health selection at migration and in immigrants' integration between European countries.

Stroke and Cardiovascular Diseases

- Okrainec et al. (2015), in an investigation from Canada with the title “Risk of cardiovascular events and mortality among a population-based cohort of immigrants and long-term residents with diabetes: Are all immigrants healthier and if so, for how long?” describe that a **lower adjusted risk of cardiovascular events or mortality was present among immigrants after accounting for differences in baseline age, gender, socioeconomic status, neighborhood, and health care utilization, which persisted beyond 10 years from immigration. However, this healthy immigrant advantage was not found among more recent refugees, immigrants with no previous education and those who were unmarried.**
- They also report that immigrants with diabetes are at lower risk for cardiovascular events and mortality compared with long-term residents, an effect that persists more than 10 years after arrival. However not all immigrants demonstrate this health advantage and further analyses need to be done.
- **The risk of stroke in migrant was extensively studied in Italy where overall stroke rates were higher in immigrant males (SHR 1.45, 95% confidence interval 1.32–1.59) and females (SHR 1.21, 1.08–1.36) with respect to the Italian population. The highest risk was observed in Sub-Saharan Africans, in both genders (males SHR 3.15, 2.62–3.76; females SHR 3.15, 2.22–4.34), followed by immigrants from South Asia and other Asian countries (Fedeli et al. 2016).**

Stroke and Cardiovascular Diseases

- Saposnik et al. (2010), in the Presario Study performed in Ontario, describe that new immigrants to North America, most of whom are under age 50 years, exhibit fewer risk factors for cardiovascular disease than their native-born counterparts.
- Vyas et al. (2020) evaluated 34,987 patients with ischemic stroke or transient ischemic attack, of whom 2649 (7.6%) were immigrants. Immigrants were younger than long-term residents at the time of stroke/transient ischemic attack (median age 67 years versus 76 years; $P < 0.001$). In the subgroup with ischemic stroke, no differences were in stroke care delivery, except that a higher proportion of immigrants received thrombolysis compared to long-term residents (21.2% versus 15.5%; $P < 0.001$). **Immigrants with ischemic stroke had a higher adjusted risk of disability on discharge (adjusted risk ratio, 1.18; 95% CI, 1.13–1.22) compared to long-term residents.** The conclusions were that "stroke care is similar in Canadian immigrants and long-term residents and that future research is needed to confirm the observed association between immigration status and disability after stroke and to identify factors underlying the association".
- **Cainzos-Achirica et al. (2019) investigated a South Asian community living in Europe, showing that they in relationship to some genetic factors and lifestyle have an increased risk for developing diabetes, atherosclerosis, dyslipidaemia, coronary heart diseases and stroke.**
- Since stroke is a multifactorial disorder, in which environmental, psychological, diet, smoking, as well as genetic factors are involved, a great improvement of prevention strategies is necessary in the immigrant communities in the different countries (Silberberg et al. 2018; Visaria et al. 2020).

Dementia

- The link of immigration as possible factor related to cognitive disorders has been recently investigated, either describing the difficulties in approaching health systems or considering the many different factors related to the pathogenesis of dementia as a possible model of interaction between brain and environment.
- Cova et al. (2020) investigated cognitive disorders in migrants through a retrospective analysis from 2001 to 2017 in a Center for Cognitive Disorders and Dementia in Milan. **Migrants with cognitive decline represented a minimal fraction (3.1%) of demented outpatients, but a grow rate of 400% was registered within the period of observation**. The correct diagnostic protocols were greatly limited by language, making it the main obstacle for the application of available diagnostic tools for dementia.
- Their conclusions were that the implementation of strategies such as transcultural diagnostic instruments and policies dedicated to this growing health problem, as well as the translation of the diagnostic tests in the different languages appear as priorities for all health systems.
- **Epidemiology of MCI in migrant populations living in Europe and estimated dementia cases have been reported by Canevelli et al. (2019a, 2020). Overall, 6,507,360 older migrants lived in Europe in 2017, 1,204,671 migrants were registered in Germany in 2010. Nearly 475,000 dementia cases (329,028 women, 147,410 men) were estimated in this population by applying age- and sex-specific prevalence rates.** When considering each European country, the number of estimated cases ranged from 108 (Iceland) to 119,161 (France). In parallel, the proportion of dementia cases occurring in migrants ranged from 0.9% (Czech Republic) to 51.2% (Liechtenstein).

Dementia

- **A similar investigation was reported for Italy (Canevelli et al. 2019b) where overall 186,373 older immigrant subjects lived in Italy in January 2017, nearly 7700 dementia cases were estimated in this population (5022 among women, 2725 among men).** When considering each specific Italian region, the number of estimated cases ranged from 19 (Basilicata) to 1500 (Lombardia) with a marked inter-regional variability.
- Wändell et al. (2019) reported data on the association between country of birth and incident dementia in several immigrant groups in Sweden. The study population included all adults (*n* = 3,286,624) aged 45 years and older in Sweden. Dementia was defined as having at least one registered diagnosis of dementia in the National Patient Register. The incidence of dementia in different immigrant groups, compared to Swedish-born individuals, was assessed by Cox regression, expressed in hazard ratios (HRs) and 95% confidence intervals (CI). All models were stratified by sex and adjusted for age, geographical residence in Sweden, educational level, marital status, and neighborhood socioeconomic status. A total of 136,713 individuals (4.2%) had a registered dementia event; 3.6% among men and 4.9% among women. After adjusting for confounders, in general, there was a lower incidence of dementia among both male immigrants (HR 0.85, 0.83–0.88) and female immigrants (HR 0.93, 0.91–0.95) compared to their Swedish-born counterparts. Among immigrant groups, a higher incidence (HR, 95%CI) of dementia was observed among men from Finland (1.14, 1.08–1.20), Bosnia (1.61, 1.18–2.20), Estonia (1.25, 1.10–1.43) and Russia (1.37, 1.12–1.69), and women from Finland (1.20 1.15–1.24) and Norway (1.14, 1.07–1.22). They conclude that the risk of dementia was lower in immigrants in general compared to the Swedish-born population; however, there were substantial differences among immigrant groups in risk of dementia. Developing dementia in a new country with a different language could cause problems for both patients and the health care staff.

Dementia

- Moon et al. (2019), investigating the prevalence of dementia by race/ethnicity and immigrant status in USA, report that **U.S.-born non-Hispanic blacks (NHBs) have a higher prevalence of dementia than U.S.-born whites, Hispanics, and others**. Immigrant status moderated the relationship between race/ethnicity and dementia. Non-Hispanic whites (NHWs), Hispanics, and other immigrants had a higher prevalence of dementia compared with their U.S.-born counterparts. However, U.S.-born NHBs had a higher prevalence of dementia compared with NHB immigrants. Older age predicted higher dementia across the four racial/ethnic groups. They conclude that "Immigrant status may have complex effects on dementia risk. Selection factors affecting immigration-varied health and educational systems in diverse countries of origin, acculturative stress, and validity of dementia assessment across diverse groups- deserve further attention".
- Gender (Tang et al. 2019), age of migration (Garcia et al. 2020), ethnicity (Petersen et al. 2020) and some genetic mutations (Arnold et al. 2013; Segers et al. 2020) have been investigated as influencing the risk of cognitive deterioration and dementia in immigrants.
- However, since cultural and environmental transcultural factors are recognized as important to modulate cognition and other brain activities, more studies need to clarify the possible link of potentially increased dementia syndromes in old immigrant populations.

Dementia

- Since 2010 (Craik et al. 2010), bilingualism has been associated with a delayed onset of dementia and may represent a cognitive reserve. This observation has been confirmed by Mendez et al. (2019) who showed a 4 years delay of Alzheimer's disease symptom presentation in bilingual individuals. The patients in advanced states of the disorder went back to the original language.
- Many recent investigations have reconsidered the association of language and cognitive impairment in aging (Brini et al. 2020; Nielsen et al. 2019; Celik et al. 2020; Berkes et al. 2020; Padilla et al. 2016) concluding that the low level of knowledge of the host country's language represents a great barrier, mainly in aged immigrant and refugees population, and may greatly influence the risk of cognitive deficiency, due to the limitation of external stimuli and comorbidity of psychiatric pathologies. On the other hand, when a good integration is present, with a good knowledge of the host country's language, a protection against cognitive loss may be present.

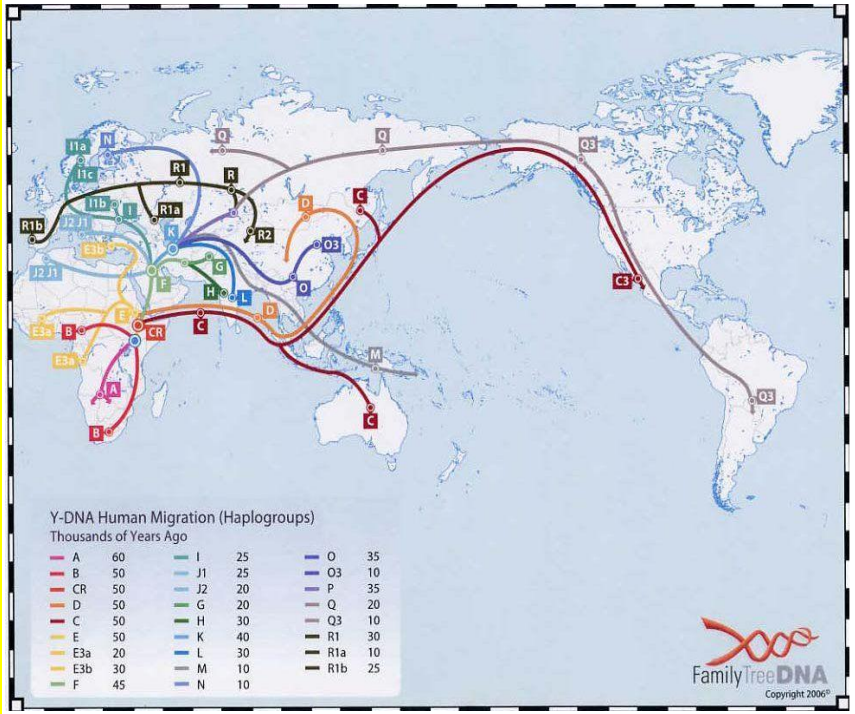
Genetic Mutation in Health and in Neurodegenerative Diseases

- Population genetics and mitochondrial DNA allotype investigations have been intensively utilized to study the origin of the different populations and migrations in the ancient ages. We know that great migrations occurred from Eurasia and Africa to Europe many century ago thanks to the study of mitochondrial DNA, that is transmitted by the mothers (see in this book, the chapters on the history of migrations).
- However, the studies by linkage analyses of great families with genetic diseases, enlarging the samples with the contribution of members of the same families who immigrated in other countries a long time ago, have had an important role defining the genetic pathogenesis of several neurodegenerative disorders, with the identifications of the gene related to the diseases.
- Examples, in the pre-genomic era, are:

1. the first presenilin mutation responsible of Alzheimer's disease described in the Volga family and linked with another family immigrated in USA (Bird et al. 1988; Yu et al. 2010);

2. the discovery of the synuclein gene as responsible of the pathogenesis of Parkinson's disease (PD) in the first great dominant PD family from Contursi (Italy), whose results have been linked with the other part of the family migrated in USA and Canada in the XIX century (Golbe et al. 1996);

3. the discovery of SCA2 gene as responsible of Machado-Joseph disease or SCA 2 ataxia, the most frequent form of dominant ataxia (SCA 2), was firstly described in families of Portuguese-Azorean ancestry, showing a founder effect spreading into the world (Martins and Sequeiros 2018; Gaspar et al. 2001).



Migration and the Risk of Multiple Sclerosis

- Migration effect on the risk of multiple sclerosis has been evaluated in many studies confirming that European and North-American immigrants had the highest prevalence of MS, whereas African and Asian immigrants had the lowest.
- **Recently Wändell et al. (2020) have reported a lower MS incidence in first-generation immigrant men (HR 0.72, 0.64–0.82) and women (HR 0.67, 0.62–0.73), and in second-generation immigrant men (HR 0.88, 0.79–0.97) and women (HR 0.79; 0.73–0.84). The evidence that recent migrating subjects differ in the MS risk from the second generation patients confirms that environmental factors may also contribute to the MS pathogenesis (Orton et al. 2010; Smestad et al. 2008; Berg-Hansen et al. 2015; Barnett et al. 2016; Nardin et al. 2018).**
- **Munk Nielsen et al. (2019) showed that first-generation immigrants arriving in Denmark before age 15 had a multiple sclerosis risk higher than that in their country of birth but lower than that in Denmark, reaching on average 69% of the multiple sclerosis risk among ethnic Danes.** Multiple sclerosis risk among individuals arriving to Denmark at a later age remained closer to that of their country of birth, corresponding to 45% of the multiple sclerosis risk among ethnic Danes. This data suggest that environmental factors may have their role in the pathogenesis of this disease in childhood or adolescence.

Migration and the Risk of Multiple Sclerosis

- These data are in agreement with analogous results performed with different ethnicity migrants in France (Nardin et al. 2018), Canada (Orton et al. 2010; Rotstein et al. 2019), Norway (Smestad et al. 2008; Berg-Hansen et al. 2015) and Australia (Barnett et al. 2016), and confirms the previous studies by Dean and Kurtzke (1971) suggesting that the incidence of MS changed in subjects who migrated from a high to low-risk country. This phenomenon was observed initially for South Africa where the MS prevalence was low in Afrikaners, highest in immigrants from Europe and intermediate in South African English.
- As reported by Milo and Kahana (2010) we can conclude that "the risk of acquiring this complex disease is associated with exposure to environmental factors in genetically susceptible individuals". The analysis of the geographic epidemiology of the disease, the influence of immigration, age at immigration, clustering and epidemics, various presumptive risk factors as ultraviolet radiation, vitamin D, Epstein-Barr virus and infectious mononucleosis, other infectious agents and non-infectious factors, combined with pathological and immunological data, may contribute to the debate whether MS is an autoimmune disease, a latent or persistent viral disease, or a neurodegenerative disease

Brain Functional MR Connectivity Changes

- Two interesting researches performed on refugees from North Korea have investigated the connectivity of the brain areas by functional MRI in subjects with different clinical situations:
- Kim et al. (2020) investigating 45 North Korean (NK) refugees and 40 South Korean (SK) natives reported that **Resting-state connectivity values from the left amygdala to the bilateral dorsolateral prefrontal cortex (dlPFC) and dorsal anterior cingulate cortex (dACC) were higher in NK refugees than in native SK.** Additionally, the strength of connectivity between the left amygdala and right dlPFC was positively associated with alexithymia score after controlling for the number of traumatic experiences and depression scores. It was found that **NK refugees exhibited heightened frontal-amygdala connectivity, and that this connectivity was correlated with alexithymia and that the higher frontal-amygdala connectivity in refugees with alexithymia may represent frontal down-regulation of the amygdala, which in turn may produce this symptom.**
- Jeon et al. (2020) studied the resting state Functional Connectivity (rsFC) of thalamus and its associations with trauma-related features (PTSD) in North Korean refugees (n = 23), trauma-exposed North Korean refugees without PTSD (trauma-exposed control [TEC] group, n = 22), and South Korean healthy controls (HCs) without traumatic experiences (HC group, n = 40). Thalamo-postcentral rsFC was positively correlated with the post traumatic scale total score in the TEC group, and with the number of traumatic experiences in the PTSD group. Negative rsFC between the thalamus and somatosensory cortices might be compensatory changes after multiple traumatic events in refugees.

Children Migration and Child Refugees

- Since children represent an important number of migrants and refugees, sometime arriving in the host country without parents, numerous reports have focused their attention on the best way to **reduce the psychological troubles that this new situation can have on their development** (Minhas et al. 2017). A specific chapter on the subject is dedicated in the book.
- A positive aspect of this dramatic situation, is the fact that intensive investigations on the pathogenetic diagnosis in many refugee children with neurodegenerative and neurometabolic diseases leads to a **correct diagnosis of rare genetic disorders, with discovering sometime new mutations, new phenotypes (Latimer et al. 2018; Schiergens et al. 2018 Hamad et al. 2020) and possibility of therapies.**

Conclusions

- It was a reciprocal positive correlation between neuro-research and migration, with results related to the focusing of needs of refugees and migrating individuals, their facility to access to host country health system, their possible different risk for diseases, as well as the role of environmental and genetic predisposition.
- The correlation with migration was also important to link some large families in order to investigate the intimate pathogenesis of disorders like Alzheimer's disease, Parkinson's disease, and ataxia.
- In this area, where political and social aspects are prominent, the use of scientific methodology will greatly help the knowledge of the correlation of this important phenomenon with brain function and dysfunctions.

Arrival of 20.000 albanian immigrants to the Bari's port on the august 8th 1991

Reality and Fiction

Lamerica

by Gianni Amelio,

movie 1994

66 Internationale Filmfestspiele Berlin
Competition
DAL REGISTA LEONE D'ORO PER "SACRO GRA"
FUOCOAMMARE
Un film di Gianfranco Rosi

Global Compact for Migration. Morocco, Marrakesh – 10/11 December 2018.

This Intergovernmental Conference is convened under the auspices of the General Assembly of the United Nations and held pursuant to resolution 71/1 of 19 September 2016, entitled “New York Declaration for Refugees and Migrants”, which decided to launch a process of intergovernmental negotiations leading to the adoption of a global compact for safe, orderly and regular migration.

In his opening statement, UN Secretary-General Antonio Guterres emphasized that the GCM is aimed in particular at the 20% (around 50 million) of illegal migrants worldwide**. It is also about avoiding human suffering during migration - over 60,000 migrants have lost their lives since 2000**. The pact is historic because it gives the UN the opportunity to work effectively with UN member states on migration issues.

The general debate was opened by 13 heads of state and heads of government: Chancellor Angelika Merkel, Lars Lokke Rasmussen, Alexis Tsipras, Charles Michel (Belgium), Pedro Sanchez Perez-Castejoin (Spain) and Cardinal Pietro Parolin.

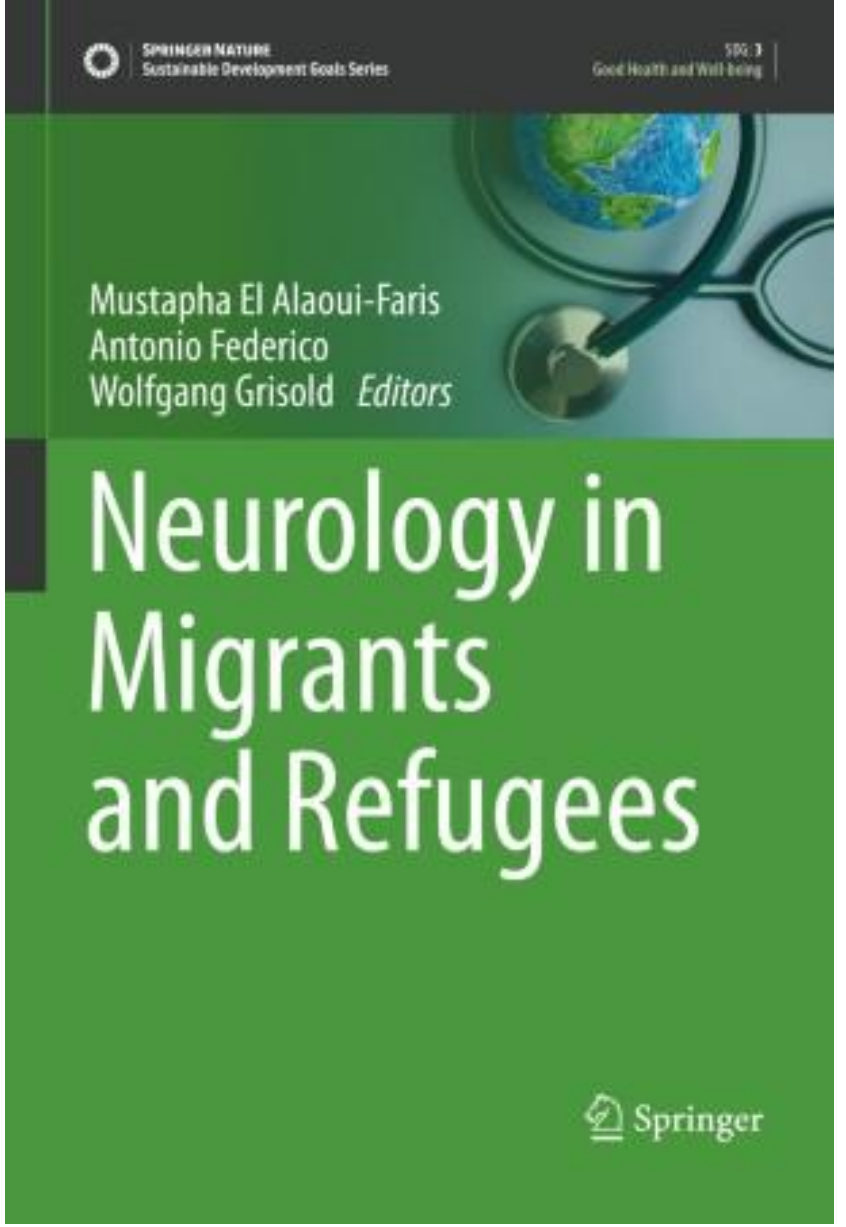
Neurology in Migrants and Refugees

Editors (view affiliations)
Mustapha El Alaoui-Faris, Antonio Federico, Wolfgang Grisold

Discusses the scientific and epidemiological data of each neurological disease in migrants

Provides practical guidelines for the diagnosis and treatment of each disease

Examines the relation between immigration and neurological diseases in migrants and refugees



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